I. SYNTHESIS AND THERMAL CHARACTERISTICS OF POLYACRYLONITRILE MODELS

II. REACTIONS OF POTASSIUM CYANIDE SOLUBILIZED IN APROTIC SOLVENTS BY 18-CROWN-6 MACROCYCLIC POLYETHER, CRYSTALLINE COMPLEXES OF 18-CROWN-6 WITH VARIOUS NITRILE COMPOUNDS, AND SYNTHESIS OF 12-CROWN-4

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SUMMARY, POLYACRYLONITRILE MODELS

In the first portion of the thesis work, novel syntheses of the pure 3-unit models of polyacrylonitrile (PAN), 1,3,5-tricyanopentane and 2,4,6-tricyanoheptane, and of the impure 4-unit model, 2,4,6,8-tetracyanononane, were developed. The syntheses were simpler, milder, and resulted in higher overall yields than older methods. Main difficulties encountered in the devised procedures were lowered yields of model due to reverse Michael addition product formation, and purification of the crude 4-unit model.

Differential thermal analyses/thermal gravimetric analyses (DTA/TGA) of the pure 3-unit models, impure 4-unit model, and PAN itself were made in an attempt to elucidate and correlate the thermal degradative mechanisms. The pure 3-unit models were found to be inadequate for comparison tests with the thermal characteristics of the polymer, exhibiting little nitrile cyclization and catastrophic weight loss in the 200-300^{o}C region. The DTA/TGA curves of the 3-unit models were independent of the atmosphere employed. The PAN examined behaved similarly to polymers reported in the literature. The impure 4-unit model exhibited thermal characteristics similar to both the 3-unit models and PAN, but resembled the latter more than the former. On the basis of the results, self-initiation mechanisms for the nitrile cyclization were rejected in favor of initiation by impurity functional

groups. Contribution to the initial exotherm by oxidative attack on the uncyclized 3-unit models was also shown to be minimal.

^{13}C-nmr spectra of 1,3,5-tricyanopentane, 2,4,6-tricyanoheptane, and simpler PAN analogs were obtained. Analyses revealed that 1,3,5-tricyanopentane exhibits a simple spectrum (no asymmetric carbons), while the ^{13}C-nmr spectrum of 2,4,6-tricyanoheptane is complex due to stereoisomers. The latter model was shown by ^{13}C-nmr to contain only 2 of the possible 3 stereoisomers as synthesized. The spectra and molecular model studies were employed to determine that the 2 stereoisomers isolated were of the racemic (atactic PAN model) and meso (syndiotactic PAN model) structures, while formation of the sterically-hindered isotactic PAN model (also meso) had apparently been selectively omitted in the synthetic path utilized.

Several significant discoveries in related chemical areas arose during the development of the PAN model syntheses. Contrary to the literature, it was demonstrated that reactive geminal, β-keto, and α-cyano esters could be decarbalkoxylated in high yields in wet dimethylsulfoxide (DMSO) without added sodium salts. Ethyl phenylmalonate was also decarbalkoxylated in dry DMSO at elevated temperatures. Possible mechanisms for the decarbalkoxylations in wet and dry DMSO were presented. It was also discovered that hydrazones and semicarbazones could be converted to the corresponding azines by simply heating in non-anhydrous DMSO. Mechanisms for the conversions were formulated.

SUMMARY, CROWN ETHERS

In the second portion of the thesis work, various aspects of crown ether chemistry were investigated. Assistance was given to the principal workers (G. W. Gokel and H. P. Harris) in improving and perfecting a novel synthesis of 18-crown-6 from commercially-available substrates under wet reaction conditions that was superior to earlier methods. The first modified Williamson synthesis of 12-crown-4 using commercially-available materials and non-anhydrous conditions was also developed. Adaptation of the 12-crown-4 system to the synthesis of 14-crown-4 was unsuccessful.

Novel crystalline, high-melting complexes of 18-crown-6 and a variety of nitrile compounds were synthesized and characterized. The complexes exhibited a range of stoichiometries and melting points. DTA/TGA, ir, and ^{13}C-nmr analyses confirmed that the crystalline solids were true complexes.

Cyanide ion was solubilized in CH_3CN (preferred) or C_6H_6 by complexation with catalytic 18-crown-6 (termed "naked" cyanide), and the anion was utilized in a variety of synthetically-useful reactions. Primary chlorides appeared to react much faster than the corresponding bromides. With secondary substrates, alkyl bromides reacted faster than the chlorides, though the latter gave a higher yield of substitution product. Reaction of cis-, trans-1,4-dichloro-2-butene with "naked" cyanide produced a wide variety of substitution and rearrangement

products. Hydrocyanation of methacrylonitrile and cyanohydrin formation with cyclohexanone were successfully performed with "naked" cyanide-acetone cyanohydrin. Decarbalkoxylation of ethyl phenylacetate was performed with "naked" cyanide or chloride in benzonitrile. Several reactions, e.g., production of substituted benzonitriles from the corresponding halides, were unsuccessful with the "naked" cyanide system. Mechanisms and postulates were derived to explain the experimental results.

Kinetic studies were performed with "naked" cyanide and several primary alkyl halides under homogeneous conditions in CH_3CN. Rate data were successfully obtained with 1-chlorohexane, which exhibited a second-order rate constant of 4.8×10^{-4} liter/mole-sec. The observance of second-order kinetics, in conjunction with the observation that 1-bromohexane reacted many times faster than 1-chlorohexane under homogeneous conditions, confirmed that the complexation-precipitation equilibrium constants for the salts present in the catalytic crown-"naked" cyanide system controlled the overall rate of reaction.

CHAPTER I

INTRODUCTION, POLYACRYLONITRILE MODELS

Historical Background, Degradation and Models of PAN

In the early development of polyacrylonitrile (PAN) as a textile fiber, much interest was created by the color changes that progressively took place in the polymer (and in the structurally-related polymethacrylonitrile) upon heating the solid material under various atmospheres at moderate temperatures or chemically-treating the polymer in solution. The color changes normally progressed through white, yellow-orange, brown, and finally, black. Interest in the degradation of PAN increased greatly with the discovery that when the polymer was heat-treated in a certain fashion under tension, it was transformed into carbon fibers without losing its dimensional stability. The carbon fibers were exceedingly strong and stiff, and were found to form an advanced type of reinforced composite when imbedded in a suitable resin polymerized around the structure. The fibers themselves possessed mechanical properties comparable to or better than common engineering materials, e.g., steel, glass, or aluminum, while the composites were superior in strength on a weight-for-weight basis to any alloy or metal known while being much lighter[1]. The composites have been used

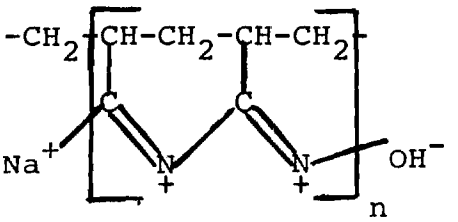
in vehicle construction (aircraft, space, and automobile industries) as well in numerous other commercial products requiring high strength and stiffness. Whereas metal properties are approaching their ultimate values, carbon fibers are in an infant stage of development and have the potential of being prepared with even more desirable mechanical properties[1].

Thus due to the commercial significance of the carbon fibers as engineering materials, considerable research has been directed toward elucidation of the mechanisms involved in converting the polyacrylonitrile structure into the graphite-related structure of the carbon fiber. In true graphite, the atoms in each plane are arranged in a similar manner with respect to those in adjacent planes, but in carbon fibers there is no such regular arrangement (the structure is termed "turbostratic")[1]. Researchers have utilized both the polymer itself and model compounds in their investigations. The following sections will summarize the results of this research, with emphasis placed on the most revealing studies of the thermal degradation of PAN and on the syntheses and degradation studies performed with PAN models. Several detailed reviews on the degradation of PAN and the development of carbon fibers and their composites have been published[1-24].

Degradation of PAN and Related Polymers

Chemical Degradation

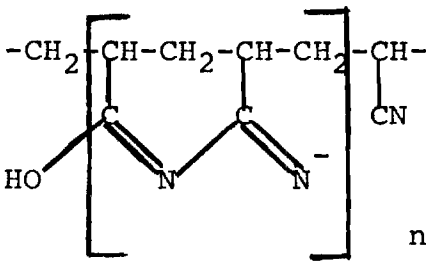
Houtz, in one of the earliest studies of PAN degradation, found that addition of aqueous, catalytic alkali to DMF solutions of PAN caused a rapid decrease in molecular weight and immediate appearance of orange color. Acidification lightened the color to yellow[25]. In a continuation of the study, McCartney concluded that the color changes did not involve degradation of the polymer chain or interaction with the solvent, but were characteristic of a reaction involving the cyano groups. Naphthyridine-type ring formation 1 was probable (similar to that postulated by Houtz[25] for the thermal degradation of PAN)[26-27]:



1

McCartney attributed the deep red-orange color exhibited by highly degraded solutions to be mainly due to reaction of the cyano groups with dimethylamine, formed by reaction of sodium hydroxide with DMF. Moore and Saito, also studying base-catalyzed degradation of PAN in DMF, retained the condensed naphthyridine-type structure of McCartney, but favored an anionic-initiation mechanism postulated by earlier

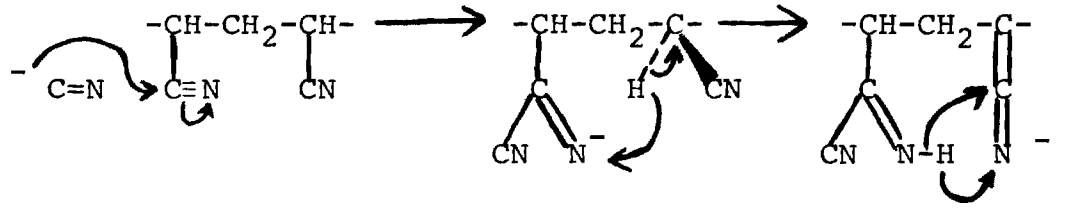
workers for degradation of polymethacrylonitrile[28-29] (PMAN) under similar conditions (propagation by imine anions), 2[30]:

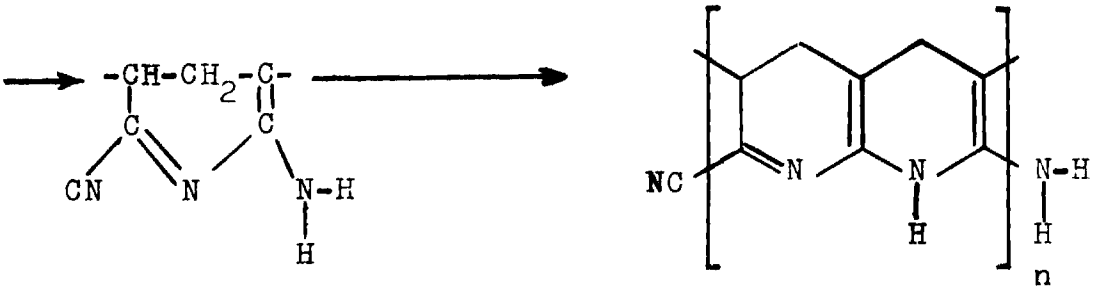


2

Ir evidence was presented to support the structure (decrease of C≡N absorption at 2222 cm^{-1} and increases of the C=N (1695 cm^{-1}) and conjugated C=N (1600 cm^{-1}) absorptions with time). The authors also found that reduction in the depth of color by addition of acid decreased with increased time of storage at 60°C before treatment. Citing the lower stability of long fused-ring structures, Moore and Saito postulated that acid-catalyzed reduction in conjugated double bond sequences was occurring. The theory was similar to that put forth earlier by Grassie and McNeill to explain the reversion of thermally-degraded PMAN from deep red to yellow on acid addition to a cyclohexanone solution[31]. Saito in a later study added uv as an instrumental tool for monitoring the degradation, and found that the alkaline discoloration decreased markedly with introduction of a comonomer, e.g., methyl acrylate, in the polymer chain[32]. Saito correlated his results with the acrylonitrile unit length, and hence to

the probability of conjugated double bond formation. Other authors have found a variety of chemical reagents that catalyze the PAN color change, including DMF alone at high temperatures[33-35], colored alkali halides obtained in the Wurtz-Fittig reaction[36], $VOCl_3$-$AlEt_3$ organometallic catalyst[37], organotin compounds[38], chlorosulfonic acid[39], dimethylsulfone at high temperatures[40], and $ZnCl_2$ at high temperatures[41]. All of the authors accounted for the color changes by invoking the naphthyridine-type ring formation of the earlier workers[33-41]. In a recent study, Potter and Scott investigated the discoloration of PAN with catalytic NaCN at 150°C[42]. Based on the extreme sensitivity to oxygen exhibited by PAN degraded under nitrogen[42] and at low pressures[43], the similarity between the cyanide- and thermally-degraded polymers, and the suggestion from model studies (not detailed) that the methine hydrogen was actively involved in the reaction, the authors postulated the following mechanism to give the repeat structure 3:





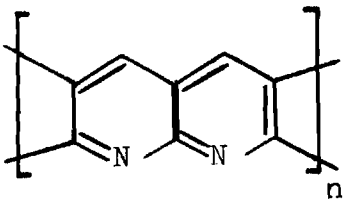
3

As supporting evidence, Potter and Scott cited earlier work that demonstrated 1,4-dihydropyridine (the model compound of 3) to be readily oxidized[43] and that showed the 1,4,4-trimethyl derivative to have ir bands in the double bond region compatible with that of the cyanide-degraded PAN (1662-1668 cm^{-1} and 1600 cm^{-1})[44].

Thermal Degradation

Houtz first studied the thermal degradation of PAN fiber in his classical investigation of the polymer[25]. Under drastic heat treatment, the polymer was shown to progress from white through yellow, brown, and black. The black yarn had surprisingly good physical properties after strenuous heat treatment (60 hr, 200°C), and was remarkably stable to further heating (little or no combustion occurring even in a flame). Elemental analysis of the flamed samples (C, H, and N) added to only 85-90%. Houtz concluded that the high tensile properties eliminated extensive polymer chain degradation (as had been observed in the alkali-degraded PAN) and that the incomplete elemental analysis indicated oxygen was

introduced. Through a series of complicated hydrogen transfers and nitrile polymerization (no imine nitrogen electron configuration postulated), Houtz speculated that the aromatic naphthyridine ring system 4 had been formed at high temperatures:

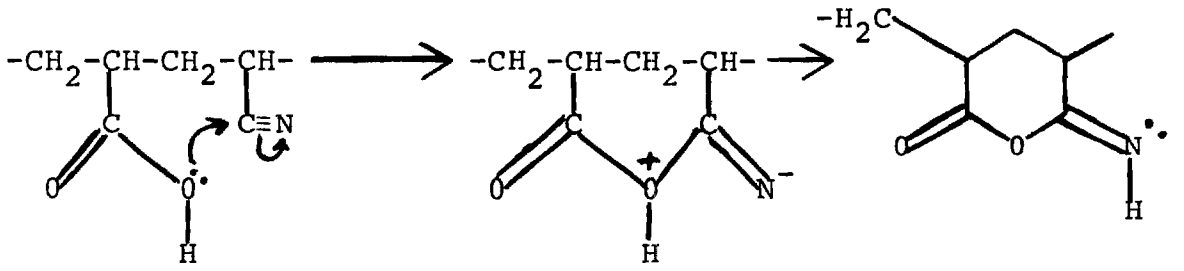


4

The theory of ring formation in thermally-degraded PAN (or slight modifications thereof) was to find utilization by numerous authors in later work concerning all types of PAN degradation.

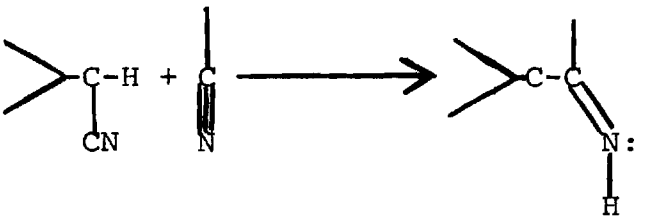
Grassie and McNeill laid the foundation for many of the later studies on PAN degradation with an excellent series of publications on the degradation of the closely-related polymethacrylonitrile. Important findings in the lengthy investigation were: (1) above 120°C (vacuum), the polymer color passed through yellow, orange, red, and deep red while the material became insoluble and infusible; (2) no appreciable gas evolution occurred until monomer began evolving at 220°C; (3) ketene-imine structures, introduced in the chain by imine radicals formed during polymerization

and having a characteristic ir absorption at 2012 cm^{-1}, disappeared above 120°C (dimerization postulated); (4) a marked decrease in the C≡N absorption (2210 cm^{-1}) and an increase in C=N and conjugated C=N absorptions (1693-1490 cm^{-1}); (5) reaction did not occur in the pure polymer below 200°C, with the presence of a copolymer impurity containing a Lewis base functionality, e.g., methacrylic acid, being necessary to effect coloration at lower temperatures, and (6) Lewis bases in solution (for example, OH^-, NH_2^-, carboxylic acid, phenols) caused similar color changes to occur in the PMAN[31, 45-49]. For the impure polymer, the authors attributed initiation of the nitrile cyclization below 200° to attack by the Lewis base to give the propagating imine 5[50]:



5

For coloration of the pure PMAN, Grassie and McNeill invoked a Thorpe-type[51] reaction to produce the propagating imine 6[49]:



6

In a later study, Grassie and Hay expanded the successful initiating reagents to include imides, amides, aliphatic amines, and aldehydes in the melt, and NaOEt, Ph_3CNa, and BuMgBr in solution[52]. The work of Overberger and coworkers on the degradation of PMAN supported that of the Grassie group[28, 53].

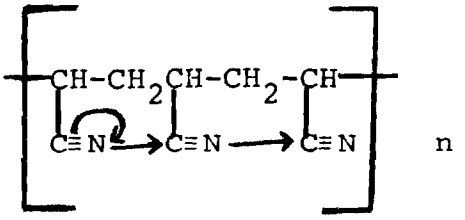
Strauss and Madorsky studied in detail the thermal degradation of PAN with precise analytical tools[54-56]. In an initial investigation (up to 500°C, vacuum), the authors collected fractions volatile at -190°C, room temperature, and only at pyrolysis[54-55]. The fraction volatile at -190°C consisted of H_2, with no NH_3 detected. The products volatile at 25°C consisted of (by mass spectra, placed in descending order of yield) mainly HCN, acrylonitrile and vinylacetonitrile, with longer reaction times yielding small amounts of pyrrole, aceto-, butyro-, and propionitriles. The waxlike material volatile only at pyrolysis was assumed to be chain fragments, with an average molecular weight of 330. Rate studies showed stabilization of the polymer at

high temperatures after short time periods. Volatilization of the polymer ceased at 70-73% of the sample weight, indicating carbonization as had been observed by earlier workers[25, 57-58]. Strauss and Madorsky attributed the rapid polymer stabilization to conjugated bond formation in the polymer backbone resulting from facile loss of HCN. The formation of acrylonitrile and vinylacetonitrile was rationalized *via* typical radical polymer degradation mechanisms such as random chain scission, β-scission, hydrogen transfers, and "back-biting"[59].

In a second study of Strauss and Madorsky, the temperature range of PAN degradation was extended to 500-800°C[56]. The effluents that were volatile at 25°C polymerized on standing and could not be analyzed. The residue after PAN treatment at 500°C varied little in elemental constituency from the starting polymer, supporting partially-hydrogenated naphthyridine ring formation[25-27]. From volatilization rate studies, the activation energy for the PAN degradation was calculated to be 31 kcal/mole. The authors postulated that crosslinking was occurring in the degraded polymer due to splitting out of HCN between intermolecular chains.

Burlant and Parsons used a variety of analytical tools to investigate the thermal degradation of PAN (200-320°C, air or nitrogen)[60]. Under nitrogen, the material was stable up to 200°C, but pyrolysis up to 320°C caused a

disappearance of the characteristic Bragg reflection of the polymer at 5.3 Å (indicating atomic disorder) and numerous ir spectra changes (disappearance of the C≡N absorption and appearance of new absorptions attributed to imine, amine, conjugated nitrile, branched unsaturates, and aromatic formation). As the pyrolysis temperature was gradually increased, elemental analysis showed the C:H ratio to gradually increase as the amount of nitrogen decreased, indicating aromaticization. Below 210°C, only NH_3 was detected as an effluent, while above 210°C HCN and also traces of aliphatic materials were found. Hydrogen was not an important decomposition product. Thus under nitrogen, Burlant and Parsons pictured thermal initiation of the nitrile link-up, 7:



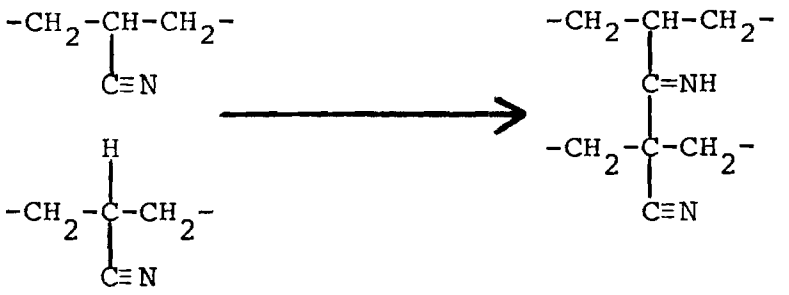
7

Further aromatization of the naphthyridine-type rings (above 300°C) was attributed to gradual loss of hydrogen[25] as well as hydrogen transfer from carbon to nitrogen. Thermal eliminations of HCN and NH_3 (from free imino groups) were considered minor reactions.

The ir spectra of PAN pyrolyzed in air were simpler, with broad, intense bands (indicative of polar bonds)[60]. A

weak carbonyl absorption was the main change in the spectra that could be determined in air. The rate of formation of HCN and NH_3 was the same in air as in nitrogen (although the polymer colored more rapidly in the former) indicating that oxygen did not activate the molecules at any point in the structure.

Schurz questioned the validity of the Houtz mechanism[25] and the subsequent modifications for the pyrolysis of PAN[61]. Citing differences in heat-and-base colored PAN, insolubility of the former, differences in the uv and ir spectra of substituted pyridines and naphthyridines and PAN, and the similiarity of discoloration of PAN and PMAN, Schurz proposed crosslinking between neighboring chains via azomethine formation, 8, to be a major reaction causing the discoloration[62]:



8

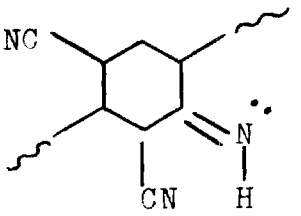
Grassie and coworkers quickly pointed out that insolubility of the heat-treated PAN may have been due to the rigidity of the new structure rather than crosslinks, that the relative ease of depolymerization of the condensed nitriles in

heat- and base-degraded PAN was probably due to the relative stabilities of terminal structures to acid, and that the proposed structure for the initial condensation product, e.g., 7, would not exhibit the uv bands noted by Schurz for the fully aromatic heterocycles[63].

Kennedy and Fontana conducted pyrolysis experiments with PAN up to 320°C under vacuum[64]. At 265°C, a minute "explosion" was visually observed, and the Bragg reflection at 5.3 Å and the ir band at 2237 cm^{-1} disappeared abruptly (as had been observed by Burlant and Parsons[60]). Solubility in DMF and specific gravity decreased (indicating ring formation), while a large decrease in inherent viscosity and a reproducible 31.6% weight loss at 265°C indicated some chain scission. The short-time reaction was attributed to reaction carriers (probably radicals) that were rapidly transmitted from particle to particle. The authors postulated that the probability of ring formation to chain scission (assuming a radical reaction for both) depended on the steric configuration of the polymer, i.e., the proportion of isotactic, syndiotactic, and atactic segments[65]. The isotactic chain segment was theorized to have the greater tendency to form a segment of fused rings, as the conjugated doubled bond structure would lie in one plane (a stable arrangement), and thus the weight loss would be a function of the degree of isotacticity in PAN.

Grassie and Hay extended the earlier work of the

group with PMAN to include the thermal degradation of PAN (200°C, high vacuum)[50, 52, 66]. As with PMAN, the rate of reaction increased with the concentration of comonomer. However, whereas coloration in pure PMAN was negligible, PAN showed a large residual rate without comonomer being present. In addition, insolubility developed in PAN (above 140°C) before coloration, while PMAN became insoluble only after excessive coloration at extreme conditions. The authors attributed the coloration of pure PAN to the labile methine hydrogen (absent in the pure PMAN) that was pictured as taking part in a self-initiation mechanism to form the structure 9:



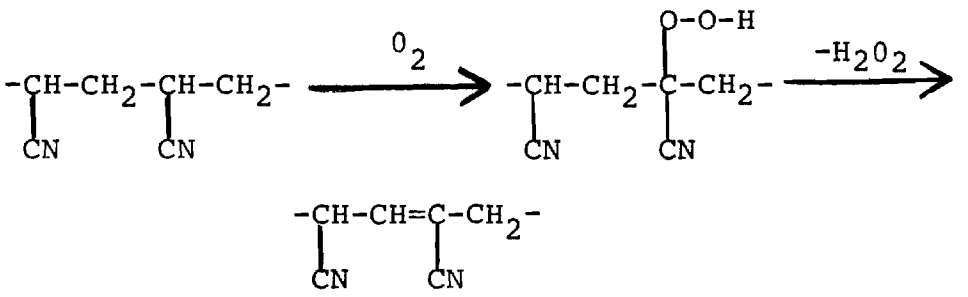
9

The imine functionality was pictured as propagating nitrile polymerization as had 5[50]. Supporting evidence was that other compounds with labile tertiary hydrogens (cumene, phenyl acetonitrile) were shown to be initiators for the color formation. The self-initiation was pictured as operating intra- or intermolecularly. This postulate, along with the more intimate packing of the PAN chains and the strong dipole-dipole interactions of the nitriles in the

polymer, were utilized to account for the ease of insolubility occurrence in relation to PMAN. Further experiments with copolymers of acrylonitrile showed that insolubility (attributed to crosslinking) decreased with increasing comonomer content and with the increasing size of the substituent of the comonomer. The comonomer effects were accounted for by a loss in close chain packing and/or blocking action of the coloration reaction along a chain. An exception was methyl vinyl ketone, which acted as an initiator in minute concentrations and apparently propagated the nitrile polymerization along the chain so that conjugation was maintained.

Conley and Bieron, using an ir null system so that only newly-formed functional groups appeared in the spectra on heating the polymer (atmospheric draft, up to 200°C), observed peak formation for internal and terminal olefins, carbonyl derivatives (acid or amide), and vinylcyanide groups[67]. Citing the intensity of the 1600 cm^{-1} band, the authors rejected the assignment of the absorption to imine linkages[60], favoring instead assignment to vinylcyanide formation. Without using the null system, the nitrile absorption band did not change during the initial oxidation stage of the reaction, i.e., the nitrile group was not involved in the process. At 160°C in vacuo or under nitrogen, only small changes were detected after 150 hr, indicating the initial reaction was dependent on oxygen. Conley and

Bieron thus pictured the initial reaction to involve attack of oxygen at the labile tertiary hydrogen with subsequent elimination to give 10:



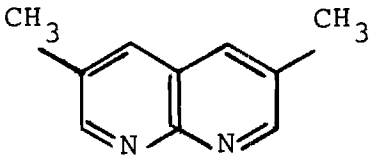
10

The structure 10 was then postulated to undergo a series of cleavages and oxidative reactions to produce the remaining functional groups formed.

At this stage of research into PAN degradation, several distinct schools of thought were developing concerning the initial process involved in the coloration of the polymer. One supported the Houtz-Grassie formation of partially hydrogenated naphthyridine rings[68-79], another the polyene structure of Conley and Bieron[80-86], and a third favored a combination of these mechanisms along with the azomethine crosslinking of Schurz occurring simultaneously[86-94]. Subsequent studies were thus mainly concerned with elucidating which of the initiation steps were predominant, how the polymerization of nitriles was propagated, the role of oxygen in the degradation, and the mechanism by which the

final graphite-like structure was formed from the oxidized polymer.

Monahan, in continuing the work of Strauss and Madorsky[54-56], fed the volatile products formed by PAN pyrolysis (280-456°C, high vacuum) directly into a vapor-phase gas-liquid chromatograph[95]. In addition to the products reported by the earlier workers, Monohan also isolated acetonitrile and cyanogen as major products, and benzene, toluene, pyridine, 3- and 4-methyl pyridines, 1,3,5-triazine, and 3,6-dimethyl-1,8-naphthyridine, 11, as minor products:



11

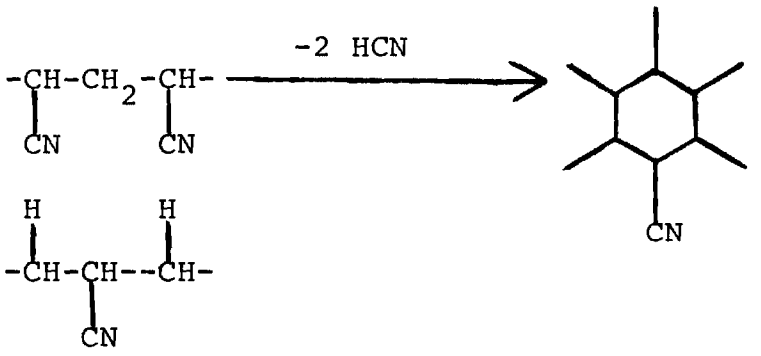
From elemental analysis of the residue (C:H:N ratio of 4:2:1) and the formation of 11, Monohan concluded that the fully aromatic ring structure of Houtz[25], 4, was correct. Ammonia was isolated only when traces of water were present, which led the author to conclude its formation was due mainly to secondary pyrolysis reactions of gases trapped in the polymer:

$$H_2O + HCN \longrightarrow CO + NH_3$$

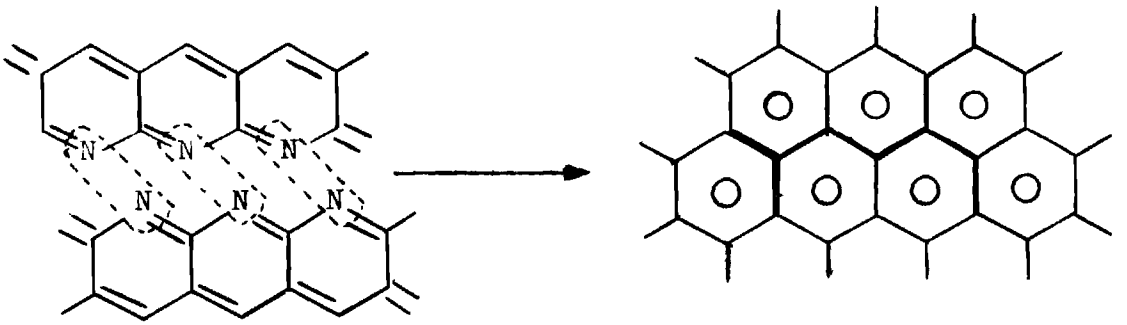
The ir and uv spectra of the pyrolyzed PAN differed little from those reported earlier[60, 62]. An interesting observation that was not pursued was that the rate of vinylacetonitrile production was proportional to the production of the pyrolyzate.

A number of other authors have also investigated gases given off by PAN during pyrolysis, both in mechanistic studies[96-112] and in studies related to the toxicity aspects of the polymer in commercial applications[113-118]. Shindo and coworkers used gas evolution techniques to study the pyrolysis of PAN in the first preparation of carbon fibers as engineering materials from the polymer, detecting mainly NH_3 and HCN[111-112]. The fibers produced by the Japanese workers, however, did not possess extreme mechanical properties. It remained for Watt, Johnson, and coworkers to discover that heat treatment of the polymer under tension through a preoxidation step (air, 200-300^{o}C), an intermediate carbonization step to eliminate most of the atoms except carbon (N_2 or Ar, up to 1000^{o}C), and a final graphitization (reorientation) step to produce the carbon fiber (N_2 or Ar, 1000-2500^{o}C) yielded a product with far superior properties to that of Shindo and also acceptable as a high-quality engineering material[8-10, 102-110]. During the studies (preoxidized or unoxidized fibers, 300-1000^{o}C, vacuum), close attention was paid to the evolution of gases, especially NH_3, CO_2, H_2O, H_2, HCN, and N_2. The Watt group

suggested that HCN elimination was a primary source of fused ring formation, 12, across chains[104]:

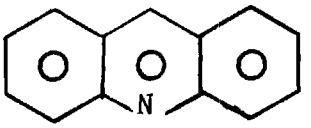


The H_2 and CO_2 evolutions were rationalized by previously proposed mechanisms[25, 66]. Nitrogen was pictured as being eliminated from the edges of the mainly-carbonized ladder polymer (700-1300°C) to go to a totally carbon, graphite-type structure 13[108]:



13

As supporting evidence, the authors cited the results reported by Marchand and Zanchetta[119], which showed that based on the electronic properties of carbon prepared from acridine, 14, there is little if any substitution of nitrogen atoms in the graphite lattice:



14

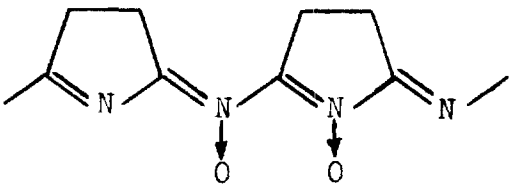
The importance of tension during the pyrolysis process has since been recognized and utilized by virtually all producers of carbon fibers with PAN as a precursor[120-148]. An extensive study of the gases released in the process (up to 1000°C) was recently performed[101]. A number of gases in addition to those already mentioned were evolved, including H_2O, CO_2, CO, CH_4, and a number of saturated and unsaturated nitriles. The pattern of gas evolution during carbonization was concluded to be influenced by decomposition reactions which caused sudden temperature increases and weight losses. Three distinct regions of gas evolution were identifiable: (1) an exothermic region (200-300°C, mainly HCN and hydrocarbons released); (2) an intermediate region (400-500°C, NH_3, CO_2, H_2O, CH_4, and hydrocarbons); and (3) a region located at 750-850°C where HCN evolution resumed and H_2 was released. From results attained with a micropyrolysis-glc technique, Bell and coworkers discovered that methacrylonitrile, but not vinyl acetonitrile[55, 95], was a major product of PAN pyrolysis, and that NH_3 was a primary and not a secondary[95] product of the degradation[149].

In a theoretical-analytical study of the thermal PAN degradation (vacuum, up to 220°C), Noh and Yu found by ir

that the disappearance of nitriles follows first-order kinetics, and that a finite amount of the groups (19-22%) remain unreacted under the conditions employed[150-151]. The first-order kinetics indicated that the kinetic chain length was very short. Using Grassie's self-initiation mechanism, 9, and a short propagation step, the authors calculated that 19.2% of the nitriles should remain unreacted, in good agreement with the experimental results. Noh and Yu concluded that the initiation step destroys 20% of the nitriles and the short propagation step 60% of the functional groups. The authors were apparently unaware that Flory had statistically calculated much earlier that the condensation of substituents X in a head-to-tail polymer of the type $-CH_2-CHX-$ was limited to 86.47% of the total due to isolation between reacted pairs[152]. Marvel, in citing Flory's work, suggested that in the pyrolysis of PAN the polymer chain would cleave by a radical mechanism at these isolated units, and thus by the law of chance, the molecular weight (MW) of the cyclized polymer will be the same regardless of the MW of the starting material[153].

Peebles, Brandrup, and coworkers published a series of excellent papers dealing with PAN degradation[154-160]. Using models for polyenes (dehydrochlorinated polyvinylchloride, β-carotene) and polyimines (polysuccinonitrile), and chemical tests for distinguishing between the 2 (Pd-charcoal hydrogenation, H_2O_2 oxidation), the authors con-

cluded that the polyene structure of Conley and Bieron[67], 10, for the initial product in the PAN pyrolysis was incorrect[154]. Subsequent workers, spectroscopically comparing pyrolyzed PAN with a polyene structure prepared by dehydrochlorination of poly-α-chloroacrylonitrile, reached similar conclusions[40, 161]. Peebles and Brandrup found that the polysuccinonitrile (formed by treatment of succinonitrile with basic catalysts[162-166]) rapidly picked up oxygen from the air when exposed after synthesis under degassed conditions. Ir, uv, and nmr data showed that the oxygen was attacking the imine nitrogen to give the conjugated nitrone structure 15:



15

Elemental analysis for polyisobutyronitrile gave C_4H_7NO for the structure, supporting 15. The inertness of base- or heat-degraded PAN to acid hydrolysis was demonstrated in conjunction with the earlier postulates of Grassie[63], supporting the imine nitrone structure (nonhydrolyzable nitrogen)[155]. The pyrolyzed PAN and the polynitrone models were both easily oxidized to colorless materials with $KMnO_4$. Uv studies revealed 2 defects in PAN polymerized by a redox

system that were identified as an enamine group (easily converted to a β-ketonitrile and an amine under weakly acidic conditions) and a β-ketonitrile group[156-157]. The formation of the defects was rationalized by production of imine radicals during polymerization with subsequent attack of residual water. Base discoloration of PAN was found to be solvent dependent, with ethylene or propylene carbonate inhibiting the reaction[156]. The model compounds 2,4-dicyanopentane, 2,3-dicyanobutane, and 2,5-dicyanohexane were thermally degraded (145°C, pure oxygen), and the rates of discoloration and oxygen uptake measured[158]. The 2,3-dicyanobutane was surprisingly found to be the most stable model to oxygen attack, and the 2,5-dicyanohexane the least stable. The authors thus concluded that the primary attack of oxygen on the PAN chain was at the methylene hydrogen to form a hydroperoxide, which in turn decomposed to a β-ketonitrile defect. Preference of the electronegative O_2 for secondary instead of tertiary hydrogen attack was attributed to the lowered electron density of the latter by the inductive (electron withdrawing) effect of the nitrile, consistent with earlier observations on similar systems[167-169]. The discoloration of the models was dependent on oxygen, as no coloration of 2,4-dicyanopentane occurred in the absence of O_2 (145°C, 1 week, pure N_2). When isobutyronitrile was thermally degraded under O_2 at 150°C, thirty compounds were detected by gas chromatography, with sixteen being characterizable[159].

The main products were acetamide, isobutyramide, N-methylpropioamide, and their acids. A polymer was isolated that was spectrally consistent with a polynitrone structure. The reactions were slow (5% conversion, 3 days), supporting the earlier evidence that the tertiary hydrogen in PAN was not overly susceptible to oxygen attack. A mechanism was devised incorporating the extensive findings of the authors for PAN degradation[160].

Attack on the cyclized structure of pyrolyzed PAN by oxygen to produce the nitrone was subject to scepticism, as the model polyimines utilized did not possess the reactive tertiary hydrogen that was inherent in the degraded polymer. Other authors have supported attack of oxygen on the partially-hydrogenated naphthyridine rings of pyrolyzed PAN to yield (after peroxide decomposition) inter-chain ether crosslinks (from both secondary and tertiary hydrogen attack)[9, 40, 103], bridging intra-ether linkages (isolated 1,3-epoxypropane units or the spiro-linked analog)[170-172], ketones (tetrahydro- and dihydro-4-pyridone repeat units)[8-9, 173], and tertiary alcohol[40]. Most of the structures, however, were based either on conjecture or spectral data (particularly ir) that was not unambiguous. Workers have recently presented evidence proposing that cyclization of the nitriles is <u>not</u> the initial process taking place in the thermal degradation of PAN[176-182]. The authors favored initial attack of oxygen on the tightly-packed PAN chains

to produce backbone unsaturation, water, and an atom of oxygen in the polymer (with hydrogen transfer to nitrogen to produce amides). Further reaction of O_2 or H_2O was pictured as producing more highly oxidized species, e.g., acids. The possibility of the presence of ionic bonds produced by hydrogen transfer from acids to amides or amines was presented. The ionic centers were pictured as initiating or catalyzing extension of the dehydrogenating centers and of aiding in alignment of the polymer chains for subsequent 3-dimensional formation. As evidence, degradation of PAN in the presence of HCl showed accelerated amine formation due to the $-NH_3^+Cl^-$ adduct (in support of Shindo's similar observations[183]) and a higher yield of carbon. Thus formation of naphthyridine-type rings by simple link-up of nitriles was characterized as a secondary reaction occurring at high temperatures, with the main emphasis in the initial degradation of PAN placed on reactions of oxygen (and released gases) in the solid-state medium[176-182]. Plausible mechanisms were presented by the authors in support of the experimental evidence and the resulting theories. In another recent series of papers, however, Fitzer and coworkers concluded that cyclization and oxidation can be considered largely independent of each other, and that most of the ring sequences are dehydrated immediately after cyclization[4-5, 184-190].

Differential thermal analysis (DTA) and thermogravi-

metric analysis (TGA) have been increasingly employed in the study of PAN degradation[40, 190-213]. Barnett first reported that a characteristic exothermal reaction occurs in PAN between 240-350°C[191], while Kennedy and Fontana attributed the exothermic transformation to cyclization of the nitriles[64]. Schwenker and Beck found a sharp exothermic transition in the DTA of commercial Orlon (an acrylic fiber containing greater than 85% acrylonitrile units) peaking at 308°C (air or nitrogen)[192]. Pure PAN gave an identical exotherm to the Orlon under N_2 except that the peak temperature was lowered to 272°C. The sudden transition was attributed to cross-linking *via* HCN elimination or nitrile cyclization. DTA/TGA combined showed a 2% weight loss within 5°C around the strong exothermic peak (vacuum)[193]. The weight loss was attributed to some chain scission to form 2-cyano-1,3-butadiene after cyclization[193,196]. Gillham and Schwenker found a correlation between sudden changes in the DTA (strong exotherm), TGA (*ca.* 15% weight loss), and torsional braid analysis (TBA, abrupt rise in modulus to a maximum) of pyrolyzed PAN around 295°C (nitrogen)[194]. Thompson observed similar changes in PAN degraded under N_2 or air, but found that the peak temperature of the exotherm decreased as the MW of the polymer decreased[195]. The exotherm was broadened considerably at various oxygen pressures, 2 maxima were visible in the DTA (250°C and 270°C), and the TGA showed a small weight gain (200-260°C) followed by a sharp weight loss dependent

on the oxygen pressures[193, 196]. The small weight gain and first exothermic peak (area independent of O_2 pressure) were ascribed to formation of hydroperoxides at tertiary carbon, while the sharp weight loss and second exothermic peak (area dependent on O_2 pressure) were attributed to oxygen uptake of residual decomposition products. The cyclization of PAN was considered suppressed due to scavenging of the tertiary hydrogens by oxygen[193, 196]. Turner and Johnson combined results from DTA/TGA (argon) with a number of other analytical tools to postulate that the strong exotherm was coincident with the nitrile cyclization even though the peak temperature depended on the rate of heating[197]. The heat of nitrile polymerization was calculated to be 5-10 kcal/mole (exothermic). Spectral changes were similar to earlier reports, while tensile and density properties showed that chain scission but not significant crosslinking had occurred. Evolution of NH_3 was attributed to a termination reaction of the nitrile polymerization. Fitzer and Mueller have recently confirmed by DTA that oxygen acts as an inhibitor of the exothermic reaction, broadening the peak considerably, and concluded that cyclization and oxidation are largely independent processes[190]. Several groups have cautioned that the position and shape of the exotherm peak in PAN pyrolysis depends on a variety of factors, including sample packing state[198, 208], oxygen concentration[198], nature of the spinning bath for the PAN precursor[202], and rate of heating[40].

DTA/TGA has been utilized to determine the melting point of PAN[210] and as an identification tool for commercial acrylic fibers[211], both dependent on the characteristic degradation processes. In crosslinked PAN fiber (hydrazine hydrate[212-213], semicarbazide[212], or thiosemicarbazide[212] as crosslinking agents), the exothermic reaction proceeded at a slower rate by DTA[213], the TGA curve was smoother[213], and heat resistances were much higher than in the initial fibers[212].

In contrast to PAN, PMAN exhibited a strong endotherm in the range 315-365^{o}C (nitrogen)[214]. No significant exotherm was observed. Almost total weight loss occurred in this region by TGA. The effect of stereoregularity on the thermal behavior of PMAN was unclear. The DTA/TGA characteristics were attributed to depolymerization ("unzipping"), an endothermic process that masked the much smaller exotherm due to nitrile cyclization[197].

Hay used differential scanning calorimetry (DSC) and thermal volatiles analysis (TVA) to study the exotherm occurring on heating PAN (vacuum or nitrogen)[215]. Volatiles were not detected in the range 130-220^{o}C, with volatiles up to 400^{o}C corresponding well with those of other workers[54-56, 95, 101]. Trimers of PAN were isolated and characterized as degradation products. DSC showed an exothermic process beginning above 240^{o}C with a maximum heat evolution at 295^{o}C. Most of the weight loss and condensate

production, however, occurred during an endothermic process that accompanied the exotherm and continued beyond it. Hay concluded that 3 distinct processes were competing, including coloration by nitrile polymerization (before the exotherm), NH_3 evolution from the coloring structures (an exothermic process), and chain scission and decomposition (exo- or endothermic, depending on the reactions occurring).

Pyrolyzed PAN has been found to be a chemical catalyst[216-229] and an electrical semiconductor[229-254] in addition to its primary end-use for carbon fiber production. Pyrolyzed PAN was found to catalytically aid in the decomposition of formic acid and hydrated hydrazine, oxidation of propylene, dehydration of cyclohexene, isomerization of butenes, dehydration of alcohols, and decomposition of hydrogen peroxide and nitrous oxide, among others[216-229]. The catalytic activity was first attributed by Manassen and coworkers to a quinoid structural unit in the pyrolyzed polymer[216-217], and later work revealed that free spins (unpaired electrons) were necessary for catalytic processes to occur[222-223, 228]. As the conductivity of the material also depended on electrons, much work has been directed towards measuring the properties of the pyrolyzed PAN[229-275]. In addition to electrical measurements (conductivity, permittivity, etc.)[229-254], other tools such as nmr[255-257], luminescence spectra (in the visible region)[258], fluorescence spectra[259], X-ray and photoelectron spectroscopy[260-266], esr[40, 267-274], and current

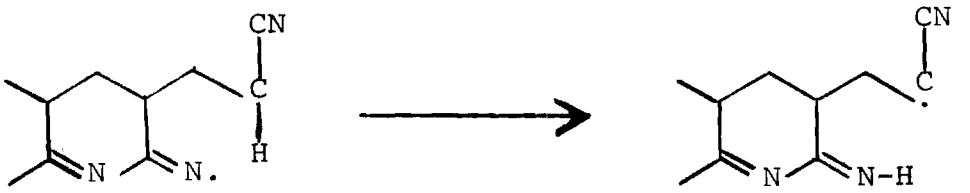
noise measurements[275] have been utilized to study the pyrolyzed materials. All of the authors retained the naphthyridine ring structures of earlier workers to explain the catalytic, electronic, or spectral observations[216-275]. An interesting discovery was that PAN formed by cobalt radiation-initiated polymerization of acrylonitrile in urea channels[245-248, 276-277] or impervious graphite[249] gave significant differences to that of bulk polymerized PAN on pyrolysis. The differences were evident in the ir spectra, DTA/TGA, and in the electrical and paramagnetic properties of the polymers. The PAN polymerized by such techniques was not amorphous[245], and hence the greater ease of carbon formation, increased conductivity of the product, and the low-temperature spectral changes were attributed to better chain packing[246-248] or increased isotacticity[254, 276-277], both of which would facilitate the nitrile polymerization. Geiderikh and coworkers showed that an increase in isotacticity decreases the induction period and activation energy of the thermal process, and the stereoregularity of the starting PAN determines the ability of the pyrolyzed material to form charge-transfer complexes[254]. Other workers found that orienting the chains by stretching the precursor fiber before pyrolysis enhanced the electrical properties of the product[250-253]. As mentioned above, Watt and coworkers made the first high-strength carbon fibers from PAN after recognizing the importance of keeping the precursor

fiber under tension during pyrolysis[8-10, 102-110]. In closely-related research, MacNulty has prepared polycyanoacetylene and found it to possess semiconductor, esr, and ir properties very similar to those published for pyrolyzed PAN[278].

Grassie and McGuchan have recently completed the most thorough studies to date on the pyrolysis of PAN and related polymers[279-287]. In the initial paper, the authors elucidated several factors that had been disputed in the earlier literature[279]: (1) the sharp, strong exotherm and deep coloration occurring around 300°C could be removed completely by isothermal ageing of PAN homopolymer (α, α'-azobisisobutyronitrile (AIBN) initiated) below 200°C, indicating a reduction in the overall conjugated nitrile sequence; (2) oxygen exhibited a marked inhibiting effect on the exotherm, and when the transition did occur at higher temperatures, the characteristics were altered such that contributing oxidative reactions were probable; (3) the degradation under N_2 occurred in the same temperature range as coloration and weight loss, indicating nitrile polymerization as the cause of the exotherm; (4) degradation under vacuum gave a much higher weight loss than under nitrogen, indicating excessive fragmentation (55% weight loss due to high MW volatiles); (5) the influence of particle size on the exotherm was negligible, while sample size was not; (6) both the sharpness and magnitude of the exotherm as well as

the amount of corresponding weight loss under N_2 were increased with heating rate, indicating that high temperature degradation was either diffusion controlled or sensitive to traces of O_2 in the gas. TVA analysis of the volatiles produced under N_2 or vacuum differed little from results of previous workers[179]. Grassie and McGuchan next investigated differences in thermal behavior of PAN polymerized by various methods (bulk (photoinitiated), solution (AIBN initiated), slurry (sodium bisulphite/potassium persulphate initiated), and anionic (lithium or barium initiated) polymers)[180]. Of the radical-initiated polymers, the slurry-prepared materials exhibited higher peak temperatures for the exotherm and increased temperatures of initial weight loss. The exotherm also occurred at a higher temperature for the bulk than the solution polymers. The anionic polymers differed greatly from the free-radical initiated materials, exhibiting relatively small exotherms under nitrogen. In air, however, the anionic polymers underwent reactions more exothermic than the solution polymers and some of the slurry polymers. Grassie and McGuchan attributed the differences in the exotherm intensity and position for the free-radical initiated polymers to the small differences in the chemical structures, resulting in differences in the ease of nitrile zip initiation and polymerization. In reference to the work of Peebles[154-160], the authors concluded that the enamine structures were more effective in bulk

polymers than ketonitrile structures in promoting the cyclization. In harmony with the work of Noh[150-151], the zip length of the cyclization was postulated to be short, but the kinetic chain length and radical activity were pictured as being maintained by transfer reactions. By this theory, the tacticity of the polymer was irrelevant to the total number of nitriles taking part in the reaction, as the structure 16 would be regenerated by hydrogen transfer upon reaching a carbon of opposite configuration:



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Structure 16 would then form the cyclohexane structure 9 discussed earlier in regards to self-initiation[66], and the chain reaction would continue. Such action would account for the residual nitriles that remain unreached in the initial degradation of PAN[150-151]. A mechanistic scheme for degradation of PAN homopolymer encompassing the accepted experimental results of the authors and others was presented[280]. Further studies showed that low temperature isothermal heating under N_2 gave the cyclized naphthyridine-type structure without a vigorous exotherm, but presence of oxygen during the preheating was necessary to prevent chain fragmentation

(presumably by oxidation and dehydration reactions occurring at the methylene unit of the ring)[281]. Various additives to PAN (selected acidic and basic organic compounds and inorganic salts) were found to cause initiation of nitrile cyclization and to broaden the characteristic exotherm with much reduced differential temperatures[282]. The weight yield of carbon was also increased in the presence of the additives, but fragmentation was not eliminated. The authors concluded that the additives could not replace the pre-oxidation step for carbon fiber production due to chain scission, but they could be used in conjunction with pre-oxidation to accelerate the process and reduce differential temperatures. Similar pyrolysis results have been reported for PAN doped with copper ions[288-289]. Comparison of the thermal behavior of PAN and of α-substituted analog polymers, e.g., poly-α-chloroacrylonitrile, showed that the substituted derivatives possessed much less tendency for nitrile polymerization[283]. The authors thus confirmed that the tertiary hydrogen in PAN plays an important role in the cyclization, presumably by hydrogen transfer to propagate the reaction. The coloration in PMAN was more intense than in PAN, although the extent of nitrile cyclization was much less. This fact indicated that -C=N- conjugation was not the total reason for coloration in nitrile-containing polymers upon pyrolysis.

The remainder of the Grassie-McGuchan papers dealt with the thermal evaluation of a number of copolymers of PAN

containing a wide variety of functional groups[284-287]. Acid and amide containing comonomers exerted a strong initiating effect on the nitrile cyclization[284]. The acidic functionalities broadened the DTA exotherm with reduced differential temperatures, chain scission, and volatilization, both in air and in nitrogen. Carbon yields were also higher than for PAN homopolymer, indicating an overall high potential for the copolymers as carbon fiber precursors. A concerted or ionic mechanism was postulated for the cyclization with acid functionalities. With amide containing comonomers, however, the exotherm was intensified in comparison to pure PAN, indicating retention of free radical initiation. In contrast, copolymers containing amideoxime structures resembled the acid rather than the amide copolymers in thermal behavior. Acrylate and methacrylate comonomers exerted a diluent effect on the exothermic cyclization without inhibiting the reaction, indicating participation of the units in the process, i.e., the reaction "passed through" the comonomer functionality[285]. Styrene-type comonomers markedly inhibited the nitrile cyclization, with the reaction blocked at the comonomer unit and the radical activity transferred to it in a chain-breaking process. Vinyl acetate comonomer also exerted a blocking effect on the nitrile polymerization, but vinyl formate, acrolein, and methyl vinyl ketone comonomers facilitated the link-up[286]. Copolymers of acrylonitrile with vinyl chloride, vinylidene chloride, and α-chloroacrylonitrile exhibited

dehydrochlorination before the nitrile polymerization occurred[287]. These comonomer units reduced the intensity of the exotherm, but did not block the nitrile reaction. Vinylidene chloride and α-chloroacrylonitrile copolymers with acrylonitrile exhibited excellent thermogravimetric characteristics, with crosslinking via the comonomer unit reducing fragmentation and carbon yields. These materials were thus also considered candidates for carbon fiber production[287]. Other studies of the thermal degradation of copolymers of acrylonitrile have appeared, including both head-to-tail copolymers (vinyl chloride[290], vinylidene chloride[290-293], styrene[294-297], methyl acrylate[298], methyl methacrylate[299], tetrafluoroethylene[300], and methyl vinyl ketone[301] comonomers) and graft copolymers (monocarboxy cellulose[302], oriented polypropylene[303], chlorinated polyvinychloride[304], and polytetrafluoroethylene[305] grafted with PAN). A review of his work on the degradation of PAN copolymers prior to 1967 has been published by Grassie[306].

Due to the commercial importance of carbon fibers from PAN precursors, much of the literature on the production of the super-fibers has been contained in patents. Although several patents have been cited herein, the scope of this review does not permit a detailed survey of the patent literature.

Light Degradation

Comparatively few authors have examined light degrada-

tion of PAN. Yoshino and Manabe found that PAN heat-treated under N_2 or vacuum was photosensitive, with the light absorption shifting to longer wavelengths and esr absorptions increasing on exposure to visible light[307]. Solubility to acids decreased for the light-exposed sample of thermally degraded PAN. The authors concluded that the incident light produced unpaired electrons in the dry-heated polymer which accelerated network formation, both at room temperature and while annealing. Hawegawa and Shimizu observed hyperfine structures (hfs) for the esr spectra of PAN degraded by uv light and γ-radiation[273]. The radicals responsible for the hfs were considered methylene and tertiary carbon radicals. A strong central line was attributed to either a free radical with many conjugated bonds of the polyene type (considered most likely) or a localized σ-type radical.

Danner and Maybeck found that irradiation of PAN film at room temperature in vacuum with polychromatic uv light caused browning and insolubility to occur[40]. New ir bands at 1630 and 3350 cm^{-1} and an esr signal characteristic of conjugated double bonds were attributed to a short -C=N- conjugated system. PAN powder degraded under similar conditions but at $77^{o}K$ gave an unresolved esr signal interpreted as a sextet due to a $-\dot{C}H_2-CH-CH_2-$ radical caused by nitrile radical formation. Initiation of nitrile polymerization was thus attributed to attack of the tertiary radical or the nitrile radical itself, although reaction of nitrile-excited groups

with neighboring nitriles was not excluded. PMAN was found to react similarly under uv light, and analogous degradation mechanisms to irradiated PAN were postulated.

Jellineck irradiated PAN in ethylene carbonate or a mixture of ethylene and propylene carbonates with a wavelength of 2537 Å at 25°C[308]. In oxygen, predominantly chain scission occurred, whereas under N_2 chain scission and recombination predominated. Under vacuum, the quantum yield was found to be 7.7×10^{-4} chain scissions per quantum absorbed. Interestingly, ir spectra indicated no change in the overall structure of the PAN after irradiation. Random breaking of carbon-carbon and carbon-nitrile bonds (assumming that the rate of breakage was proportional to the number of bonds present at any time and to the light intensity) satisfactorily explained the results. Rate constants derived by such theory were linearly dependent on the light intensity.

In a comparison of the semiconducting and catalytic properties of thermal and light degraded PAN, Lescinsky found that in contrast to heat-treated PAN polymer irradiated with a mercury lamp gave no new absorption bands, while absorption in the 210-700 nm range increased linearly[228]. Both types of degradation turned the polymer brown, but only thermal degradation gave free radicals, conjugated systems, and catalytic and semiconducting properties. Lescinsky concluded that laser degradation employing thermal radiation components would be suitable for producing semiconducting-catalytic ma-

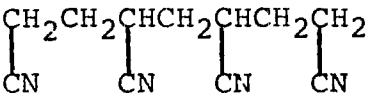
terial from PAN.

Gaulin and McDonald found that irradiated PAN fibers exhibited the characteristic DTA exotherm at significantly lower temperatures on subsequent pyrolysis than unmodified PAN[309]. Where the exotherm did not occur, the corresponding weight loss also was absent, and a high carbon yield resulted.

Models of Polyacrylonitrile

Syntheses

In his classic study of PAN and its properties, Houtz compared the ir spectra of the polymer, 1,3,5,7-tetracyanoheptane (17, 4-unit model without end methyls), 1,3,5-tricyanopentane (18, 3-unit model without methyls), and 1,3-dicyanopropane[25]:



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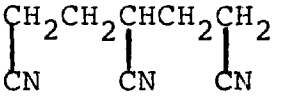

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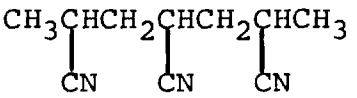
No syntheses of the models were published, however. Several authors isolated 3-carbethoxy-1,3,5-tricyanopentane (a precursor of 18) while attempting to synthesize ethyl-2,4-dicyanobutanoate by base-catalyzed Michael addition of ethyl

cyanoacetate with acrylonitrile[310-314]. Although Rogers and Lewiston obtained a mixture of the mono- and diadducts (catalytic NaCN, 150-165°C)[310], the other workers using different base systems obtained the diadduct even in the presence of a large excess of ethyl cyanoacetate[311-312]. Hawkins and coworkers produced 1,3,5,7,9-pentacarbalkoxy-1,3,5,7,9-pentacyanononane by base-catalyzed addition of formaldehyde to various cyanoacetate esters[315-316].

Zahn and Schafer published the first detailed syntheses of PAN models, including 17 and 18[317]. Utilizing the observations of the earlier workers[310-312], the authors synthesized 18 by first producing 3-carbethoxy-1,3,5-tricyanopentane from ethyl cyanoacetate and acrylonitrile in a single step (dioxane, catalytic 30% KOH-MeOH, no external heat, 2 hr). Recrystallization from ethanol reportedly gave a 97% yield of product. The ester was converted in succession to the potassium salt (ethanol, KOH, less than 50°C, until neutral) and the carboxylic acid (water, concentrated HCl, 70% from the ester), and the acid was then decarboxylated to 18 (pyridine, catalytic Cu powder, reflux (110°C), 45 min) in 29% overall yield. For synthesis of 17, the authors first produced 1,3-dicarbethoxy-1,3-dicyanopropane by either addition of formaldehyde to ethyl cyanoacetate (catalytic piperidine, 2 hr cold followed by 12 hr at reflux, 42% yield) or by the displacement reaction of ethyl cyanoacetate anion on methylene bromide (EtOH, NaOEt, 3 hr at room temperature followed by 4 hr of re-

flux, no yield reported). A di-Michael addition was then performed with the diester and acrylonitrile similar to the synthesis of 3-carbethoxy-1,3,5-tricyanopentane to give 3,5-dicarbethoxy-1,3,5,7-tetracyanoheptane (47%). The diester was converted to the alkane 17 as with 18, e.g., via the potassium salt and dicarboxylic acid (14% from the diester). The models were later used as comparison compounds for attempted identification of liquid nitrile products isolated from the thermal degradation of PAN at 550°C[318]. Attempts to obtain low MW models of PAN by controlled stepwise polymerization of acrylonitrile were unsuccessful, with three oligomeric fractions with degrees of polymerization 6, 7, and ten isolated[318-319].

Takata and coworkers published the most extensive study of the syntheses of PAN models to date[320-322]. Syntheses of 2,4,6-tricyanoheptane (19, 3-unit model with end methyls) and 2,4,6,8-tetracyanoheptane (20, 4-unit model with end methyls) was presented in the initial paper[320]:



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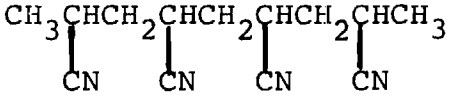


20

A Michael addition similar to that used by Zahn and Schafer in the preparation of 18[318], but with methacrylonitrile and ethyl cyanoacetate instead of acrylonitrile, produced ethyl-2,4-dicyanopentanoate (EtOH, 1 equivalent NaOEt, 75-78°C, 4 hr, 70%). The ester anion was reacted with 1-chloro-2-cyanopropane to give 4-carbethoxy-2,4,6-tricyanoheptane (EtOH, NaOEt, 30 min, 70-75°C). The material was recrystallized from ethanol (73.5% yield), converted to the potassium salt and then the acid in procedures similar to those Zahn and Schafer[318] (64% from the parent ester), and the acid decarboxylated to 19 (200°C (oil bath), 5 mm Hg, 54% from the parent ester). By reacting 2 mole equivalents of the anion of ethyl-2,4-dicyanopentanoate with 1 equivalent of methylene bromide (EtOH, NaOEt, sealed tube, 90°C, 4 hr), the authors synthesized crude 4,6-dicarbethoxy-2,4,6,8-tetracyanononane (75%). The crude product was reported to be undistillable, apparently due to its high MW and polarity. The crude diester was converted to the potassium salt (76% based on the diester) and the diacid (91% based on the salt) in the usual manner[318], and the diester decarboxylated to give 20 (Cu powder, vacuum, 200°C, 4 min) in a 34% yield from the diester. Ir spectra[320] showed that both 19 and 20 (particularly the latter) contained impurities, with bands at ca. 3500 (N-H or O-H), 1750 (C=O), and 1620 (C=N or C=C) cm^{-1}. Elemental analyses were the only precise analytical data reported by Zahn and Schafer for 17 and 18, with no spectral tools employed[318], and thus

no analogy could be drawn between the two procedures with respect to impurities in the models. While 20 was reported as a wax-like solid, 19 crystallized on sitting for long periods[321].

Fractional crystallization of 19 was subsequently conducted from MeOH to produce 3 compounds (mp's of 37-39°C (74.4%), 80-81°C (3.6%), and 45-46°C (22%)), one of which was reported to be optically active[321]. Takata reported X-ray and ir data for the fractions, and claimed that they represented the three possible stereoisomers of 19 (syndiotactic (meso), isotactic (meso) and atactic (racemic overall) isomers), although the configurations of each fraction were not elucidated. During studies on the high-resolution ^{1}H- nmr of PAN[323-324], Murano and Yamadera related the spectra to that of 19 and 2,4-dicyanopentane[325-327] (the latter also investigated in a similar study by Matsuzaki and coworkers[328]). The models were synthesized after Takata and Taniyama[320], and the fractional recrystallization from MeOH[321] for 19 repeated with minor modifications[326]. From careful analysis of the high resolution nmr absorptions of the methylenic protons of the separated components, the isotactic (uncrystallizable), syndiotactic (needles, mp 79°C), and atactic (grains, mp 53-54°C) fractions of 19 were identified[327]. For atactic 19, 2 methylenic absorptions were present due to the meso and racemic nature of the methylenes located at opposite ends of the molecule. Takata also separated 20 into 3 components by frac-

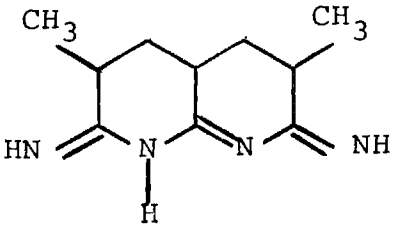
tional recrystallization from ethyl acetate (waxy solid (87.2%), and two crystalline forms (mp 158°C (4.5%) and mp 130-135°C (8.3%))[321]. As with the 3-unit model, one of the crystalline compounds was claimed to be optically active, the fractions were attributed to the various possible steroisomers of 20 (through not characterized as such), and ir and X-ray data was provided. Subsequent work by the group resulted in syntheses of model copolymers of PAN, i.e., with nitriles at various positions in 19 and 20 replaced by acid, ester, or amide functionalities[322].

Vosburgh and Green published a synthesis of 17 that was similar to that of Zahn and Schafer[329]. In the initial step, ethyl cyanoacetate was condensed with formaldehyde at less than 50°C (catalytic KOH/EtOH) to give, 1,3-dicarbethoxy-1,3-dicyanopropane (73%). If the temperature was allowed to rise above 50°C, α-cyanoethylacrylate was produced, which polymerized on distillation. Di-Michael addition of the product with acrylonitrile (60%), conversion of the 3,5-dicarethoxy-1,3,5,7-tetracyanoheptane to the potassium salt (24%) and it to the corresponding acid (60.6%), and subsequent decarbalkoxylation of the diacid to produce 17 (27.2%) followed the general routes of Zahn and Schafer[317].

Degradation

Having successfully synthesized the models of PAN and its copolymers[320-322], Takata investigated the chemical and thermal stability of the compounds in comparison to that of

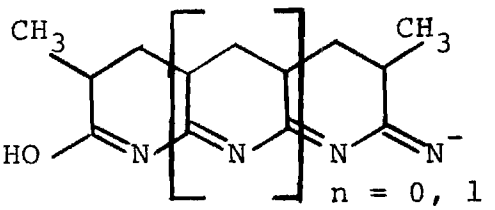
PAN[330-335]. Solutions of 19 and 20 in DMF, when treated with catalytic KOH/EtOH, turned yellow and orange respectively, and exhibited a band in the uv spectra at 265.6 mμ that increased with time. A peak that reacted similarly was located at 310 mμ in the spectra of the degraded 4-unit model. The compound 3,6-dimethyl-2,7-diaminooctahydro-1,8-naphthyridene, 21, was synthesized independently by treating 19 with $NaNH_2$ in formamide (25°C, 2 days, 83.2%), and the uv spectra shown to be similar to that of the degraded solutions of 19 and 20:



21

Also, the ir of 21 was similar to that of PAN degraded in DMF-base solution. The synthesis of 21 was later presented as a new preparation for the compound, which itself was converted by successive hydrogenation, elimination of NH_3, and dehydrogenation to 3,6-dimethyl-1,8-naphthyridene[335]. In a continuation of the study, 19 and 20 were treated with KOH in ethanol[331]. An uv absorption peak at 233 mμ shifted to 244-245 mμ, and a peak at 292-294 mμ appeared upon degradation. An additional peak at 336 mμ appeared in the spectra of degraded 20. The spectra was attributed to the formation

of 22:

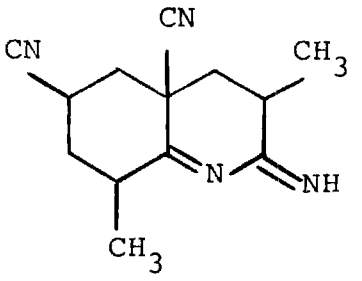


22

Ir spectra of 2,4-dicyanopentane degraded in a similar fashion gave new peaks at 1670, 1635, and 1575 cm^{-1}, consistent with the hydroxy-imine anion structure. Model compounds for acrylonitrile-acrylamide copolymer was also examined, with the conclusion that when an amide pendant group was present in the models, attack of the hydroxide ion occurred preferentially at the amide, followed by cyclization[331].

Thermal degradation of the PAN homo- and copolymer models was also investigated by Takata[332-334]. The components obtained from fractional recrystallization of 19 and 20 were used in the study[321]. The models were heated between 200-300°C in a sealed glass tube, and the reactions followed by uv and ir. The ir spectra of the degraded samples were similar to that of PAN pyrolyzed under the same conditions[334]. Although no attempt was made to isolate cyclized products from the residue or to analyze gases evolved, Takata claimed from the spectral results that the self-initiation mechanism of Grassie (see structure 9) had not taken place in the degradation of 19, but had resulted in the formation of 23 from

20:



23

Absence of a new uv absorption appearing at 259 mμ was concluded to be proof that the azomethine structure of Schurz[61-62], 8, was not formed on thermal degradation of the models. Subsequent thermal studies with PAN copolymer models indicated that all functional groups (methyl ester, acid, or amide) initiated glutaroimide ring formation, presumably by the anionic mechanism of Grassie and McNeill[50] (see structure 5)[333].

Uses of PAN Models

As the syntheses of PAN models 17-20 were developed, comparison of a variety of the model properties (other than degradation characteristics) with those of the polymer were made. Phibbs found that the relative solvent powers of liquids for 18 and PAN were qualitatively the same, and DMF was found to an acceptable solvent for both the model and the polymer[336]. DMF was eventually chosen as the solvent for PAN in commercial production of Orlon. The 3-unit model 19 was compared to PAN in the relative transport constants in solu-

tion[337]. As noted earlier, Houtz compared the ir spectra of 18 with PAN[25], and Peebles and coworkers used shorter-length models in their classic studies[154-160]. More recently, Levites and coworkers have compared the interaction of H_2S with nitrile groups in PAN by studying the thioamidation of 19[338].

In addition to the ^{1}H-nmr comparisons[323-328], the reported ^{13}C-nmr spectra of PAN[339-341] were compared to the proton-decoupled pulsed Fourier ^{13}C-nmr spectra of meso and racemic 2,4-dicyanopentane (30°C, 25.15 MHz)[342]. The chemical shifts of the model carbons were in the order CN, CH_2, CH, and CH_3 (highest to lowest chemical shift relative (ppm) from TMS). As characteristic of the ^{13}C-nmr of pairs of stereoisomers[343], the authors found that the carbons of the meso isomer absorbed at different chemical shifts from those of the d,l-pair (1.86-0.44 ppm difference, depending on the carbon involved). Significantly, the meso nitrile carbon absorbed at a lower field than the racemic analog, while the meso methine carbon appeared at a higher field than the corresponding racemic carbon. The characteristics of the ^{13}C-nmr spectra of the models coincided well with that of syndiotactic and isotactic triads of PAN in position and order of carbons[342].

Syntheses of PAN Models, Related Chemistry

Introduction

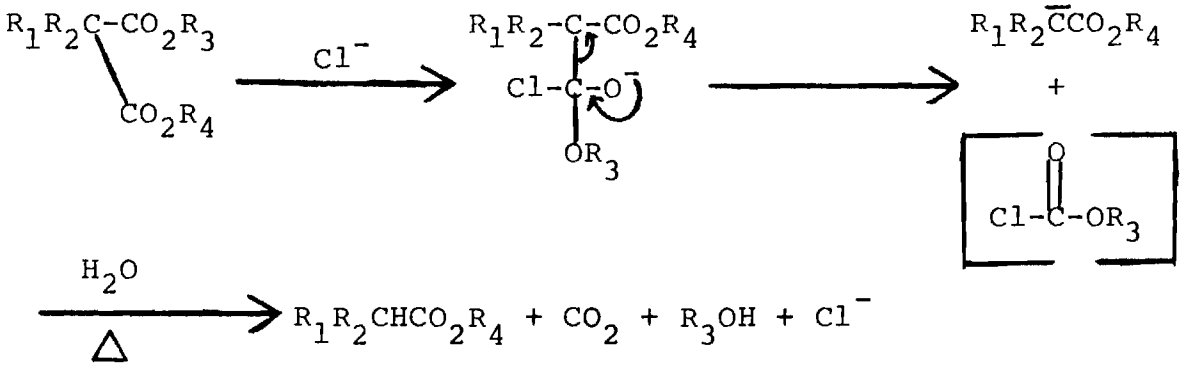
It was evident from the reported syntheses of PAN

models[317-322, 329] that the main common deficiency in all of the procedures was the difficulty in converting the intermediate esters to the nitrile models. The strenuous procedures involved both base and acid treatment, either of which can hydrolyze nitriles to amides or acids under harsh conditions[344]. In addition, the high temperatures used in the decarboxylations have been shown to cause extreme degradation of the polymer over prolonged periods[281]. The primary objective in developing new, improved syntheses of PAN models, therefore, was to perfect a mild decarbalkoxylation procedure whereby the precursor esters could be converted in facile fashion to the models in one step. Research in this area led to an unexpected synthesis of azines. The following sections will therefore briefly review the literature on decarbalkoxylation to reactive esters and classical azine syntheses.

Decarbalkoxylation of Reactive Esters

Of the few methods discussed in the literature for decarbalkoxylation of esters, the most likely candidate for use in the syntheses of PAN models was that developed by Krapcho and coworkers[345-346]. Early research demonstrated that reactive geminal diesters were converted to the monoesters smoothly and in good yields in (excess) NaCN-DMSO (160°C, 4 hr)[345]. Subsequent workers successfully utilized the procedure to decarbalkoxylate reactive esters[347-350]. The Krapcho group reported an improvement in the method by substitution of NaCl for the toxic NaCN (H_2O-DMSO, 140-183°C,

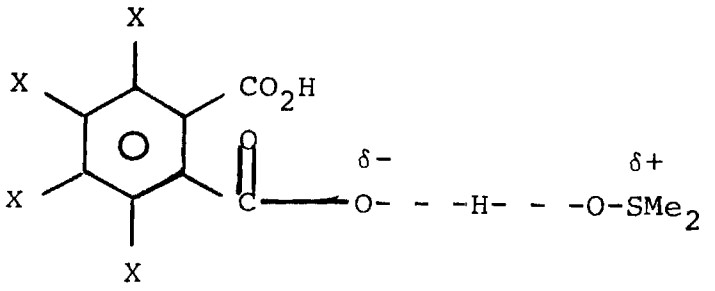
2-6 hr, excellent yields), and expanded the substrates to include β-keto esters and α-cyano esters (including ethyl cyanoacetate and ethyl-2-cyanohexanoate)[346]. A proposed mechanism that accounted for the experimental observations was presented (shown for the diester)[346]:



Successful decarbalkoxylations with alkyl metal fluorides, bromides, chlorides, sodium azide and phosphate, and with other dipolar solvents besides DMSO were reported, but not detailed[346]. In a related study[351], Wilczynski concluded that catalytic halide ion decarbalkoxylation of N-carbalkoxy pyrazoles initially involved second-order rate determining nucleophilic attack of the halide anion at the α-carbon of the ester alkoxyl group to give CO_2, an intermediate pyrazolyl anion, and an intermediate alkyl halide. The remaining step pictured nucleophilic attack of the anion on the alkyl halide to give N-alkyl pyrazole and regeneration of the halide anion.

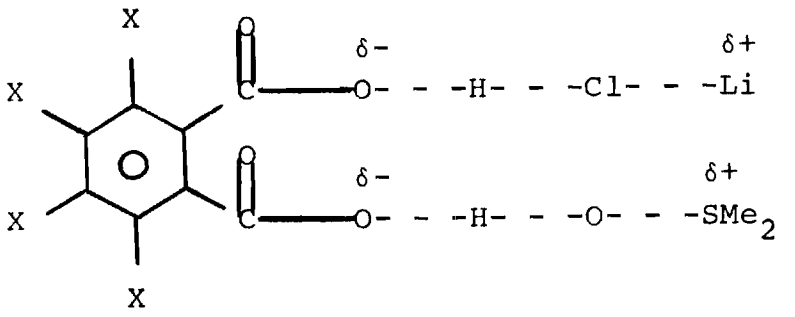
In the more recent publication[346], Krapcho claimed that water was necessary to effect the reaction with NaCl, and that

chloride ion was a necessary reagent. In support, Muller and Siegfried found that in the decarbalkoxylation of 2-benzyl-2-carbmethoxycyclopentanone in hexamethylphosphoric triamide (HMPA), the relative reactivities of NaCN, NaCl, and NaBr towards the substrate were 65, 2.45, and 1.0 respectively[352]. Attack of the halide ion to form the carboxylate followed by decarbalkoxylation was not ruled out, though concerted ester cleavage and decarbalkoxylation was also considered plausible. The authors were apparently unaware that Chen and Yan had found that tetrahalophthalic acid mono-decarbalkoxylated smoothly and in high yields in refluxing DMSO alone (30 min)[353]. The intermediate species 24 was postulated:



24

In the presence of alkali and alkaline earth salts, di-decarboxylation occurred, while in the presence of other salts, mono-decarboxylation was observed as with DMSO alone. The performed monoacids further decarboxylated when alkali or alkaline earth salts were utilized with DMSO. For the di-decarboxylations, the intermediate 25 was pictured:



25

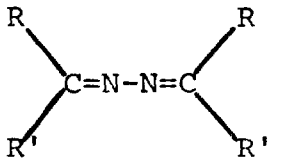
Recent studies (including a publication concerning results detailed herein[354]) have shown that reactive geminal, β-keto, and α-cyano esters, e.g., diethyl phenylmalonate, can be decarbalkoxylated in dry or wet DMSO without added halide ion[354-355]. Krapcho and coworkers, however, showed that less reactive substrates, e.g., mono- and dialkyl substituted malonate esters, show a markedly accelerated rate of decarbalkoxylation in the presence of halide anion[355].

Reservations existed on utilizing the Krapcho method for decarbalkoxylating the PAN model ester precursors[346]. Although several α-cyano esters had been examined by Krapcho[346], none were polynitriles capable of undergoing the characteristic cyclization reaction of base or thermal degraded PAN or PMAN. Chloride ion has been found to promote faster elimination from certain alkyl halides and sulfonates than alkoxides in alcohol[356], indicating the strong basicity of the anion in dipolar, aprotic solvents. Thus the possibility existed of reverse Michael addition[357] occurring with the

models due to chloride ion functioning as a base. Head and McCarty found that pure, dry DMSO heated at 180°C for 68 hr in air or oxygen was completely decomposed (5 products isolated)[358]. Various radicals, cations, and radical-anion intermediates were postulated as being formed during the degradation, several of which could conceivably initiate nitrile polymerization. Despite these possible weaknesses, however, the Krapcho decarbalkoxylation procedure offered the most attractive procedure for possible utilization in the PAN model syntheses.

Azine Syntheses

Many methods have been utilized for preparing azines of the general structure 26[359-384], including direct conversion of ketones or aldehydes by hydrazine or its derivatives[361-366], conversion of the preformed hydrazones[367-370], treatment of carbonyl compounds with NH_3 -H_2O_2 and a nitrile[371] or alkali metal compounds[372], with NH_3 and peroxycarboxylic acids[373-374], with $ClNH_2$-NH_3 and a strong base[375], and with NH_3-O_2 with $ZnCl_2$ or $CuCl_2$ catalysts[376], reduction of nitriles with N_2H_4 and Raney nickel[377-379], treatment of substituted diazomethanes with boron trifluoride etherate[380], condensation of imines with hydrazones[381] or N_2H_4[381], dimerization of ketimine magnesium halides by oxidation in the presence of $CuCl_2$, $CuCl_3$ or $FeCl_3$[382], and base-catalyzed isomerization of allyl hydrazones[383-384]:



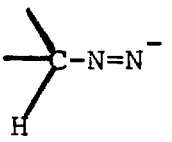
R = alkyl or aryl

R' = alkyl, aryl, or H

26

By far the most widely used procedures have been the first 2 listed above[359-370], although reduction of nitriles with N_2H_4-Raney nickel has gained some support as a general azine synthesis in recent years[377-379]. Several extensive reviews have been published concerning azine preparations[359-360].

While investigating a new, mild Wolff-Kishner reduction effected by treating hydrazones with sublimed potassium tert-butoxide in anhydrous DMSO (25°C), Cram and coworkers found that the corresponding azines were formed as side products in addition to the desired alkanes[385]. The amount of azine collected was minimized by extremely long addition times for the hydrazone (22% yield of benzophenonazine isolated if a 0.5 hr addition rate was used, while an 8 hr rate reduced the yield substantially). No mechanism was postulated for formation of the azine, though base-initiated formation of the anion 27 followed by loss of N_2 was pictured as being the route of reduction followed to produce the alkanes:



27

Kochetkov and Vorotnikova, in attempting to form phthalazine by treatment of the acetylhydrazone of benzaldehyde with HCl in anhydrous, refluxing isoamyl alcohol, unexpectedly isolated benzalazine instead[386]. The procedure was shown to be general for several substituted acetylhydrazones. Formation of the azines was attributed to alcoholysis of the acyl radical by HCl-alcohol to form the free hydrazone, followed by subsequent disproportionation of the hydrazone to the azine.

Purpose of Research

Due to the extensive but contradictory degradation studies performed on PAN and related polymers, it was decided to investigate the thermal characteristics of the 3-unit (with (19) and without (18) end methyls) and 4-unit (with end methyls, 20) models of the polymer. Many of the literature discrepancies had arisen due to the complex reactions occurring in the solid-state medium of the polymer, e.g., secondary reactions with trapped gases[176-182], and the inabilities of present analytical tools to distinguish between these reactions. It was felt that the simpler models offered a greater possibility of evaluating the thermal characteristics of polynitriles than PAN itself. Although several

groups had reported model syntheses[317, 320-321, 329], the procedures were multi-step and harsh in nature, resulting in low overall yields of impure products. The first objective, therefore, was to develop a short, mild procedure for preparation of the pure PAN models 18, 19, and 20. As the major deficient area in the older methods was in converting the ester precursors to the alkyl nitriles, priority was placed on perfecting a mild, 1-step ester decarbalkoxylation that would not affect the nitrile functionalities. Adaptation of the Krapcho procedure[346] was selected for detailed investigation. Studies of the interaction of the chloride ion in the Krapcho procedure with semicarbazones was also planned.

Although thermal and base degradation of 19 and 20 had been investigated by Takata[330-335], the studies were incomplete in a number of areas. For example, conclusions from the thermal degradation such as the existence or absence of the Grassie self-initiation mechanism[66] were based totally on questionable uv or ir spectra[332-334]. Claims of isolation of optically-active products from syntheses involving only optically-inactive reagents also cast doubt on the Takata results[321]. As DTA/TGA had proven a powerful tool for investigating PAN thermal degradation[40, 190-213, 279], the thermal method was chosen for analyses of the models in comparison to PAN homopolymer under similar conditions and with literature reports of the DTA/TGA of PMAN[197, 214]. Absence of the strong, sudden exotherm observed in the DTA of PAN in the

250-350°C region (attributed mainly to nitrile cyclization[279]) would indicate a lack of similar reactions predominating in the models. In addition, comparative DTA/TGA of pure and impure models (the latter containing amide and/or acid impurities) would shed light on the comonomer functionality or impurity initiation theories of Grassie[284-287] and of Peebles[154-160]. Lack of an exotherm for the pure models would dictate against the self-initiation mechanism of Grassie[66] (see structure 9), while presence of an exotherm or a broadened exotherm with the impure models would support the necessity of other structures in the polymer to initiate significant nitrile cyclization.

A weak or no exotherm, with drastic TGA weight loss in conjunction with a DTA endotherm, would dictate chain scission (and/or volatilization for the models) as the main thermal process occurring, e.g., as in the unzipping of PMAN[197, 214]. Comparative DTA/TGA experiments under dry air and nitrogen were also planned in order to evaluate the effect of oxygen on the model graphs with respect to changes seen in those of the polymer using various atmospheres[40, 190-215].

Although ^{13}C-nmr spectra of the 2-unit model of PAN had appeared[342], no reports of the corresponding analyses with the 3-unit models had been published. As ^{13}C-nmr had been shown to distinguish between pairs of stereoisomers[342-343], it was postulated that spectra of the synthesized mixture of 19 stereoisomers would reveal information concerning the stereo-

chemical course of the synthesis utilized. Therefore, a final objective was to analyze in detail the ^{13}C-nmr spectra of pure 18 and 19 and to compare the spectra of the latter with that observed for PAN[339-341].

CHAPTER II

EXPERIMENTAL, POLYACRYLONITRILE MODELS

Instrumentation and Apparatus

Visual melting points of the synthesized compounds (contained in capillary tubes) were determined on a Mel-Temp device. All reported boiling points and melting points were uncorrected. Infrared (ir) spectra were obtained with a Perkin-Elmer Model 237B Spectrophotometer (neat film/NaCl plates (liquids), KBr pellet or DTA (solids)). The 1601.4 cm^{-1} absorption of polystyrene was used as a reference peak in all of the ir spectra. Proton nuclear magnetic resonance (nmr) spectra were secured with either a Varian Model A-60 or T60-A spectrometer utilizing external (12% $CHCl_3$ solution) or internal tetramethylsilane (TMS) as a standard. A JEOL PFT-100 Fourier Transform Spectrometer (TMS internal standard) was employed to obtain proton-decoupled ^{13}C-nmr spectra by signal averaging. Mass spectra were obtained with a Varian Model M66 or Hitachi Perkin-Elmer RMU-7L instrument. All elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Georgia. Weights were determined on either a Mettler Type H15 or Type B6 balance. Differential thermal analysis (DTA) and thermogravimetric analysis (TGA) of polyacrylonitrile and its models were performed on a Mettler Thermoanalyzer II instrument equipped to plot simultaneous DTA/TGA

curves. Constant instrument settings for the DTA/TGA experiments were a TG sensitivity of 100 mg/in, a gas flow rate of 6 lb/hr, a DTA sensitivity of 50 μV/in, a temperature recording of 2 mv (10 mv full scale, and a chart speed of 12 in/hr. A constant-temperature silicon oil bath was equilibrated and regulated by a Thermo-Watch Constant Temperature Control (Fisher, range of ± 0.25°C). Thin-layer chromatography (TLC) was performed by the method of House[387], using both 1" x 3" and 50mm x 200mm glass plates. Glass apparatus designated as "dry" and utilized in the reactions performed under anhydrous conditions was cleaned thoroughly, rinsed with acetone, and dried in an oven at 110°C for at least 12 hr before use. After removal from the oven and assembling, the apparatus was flamed out with a Bunsen burner under nitrogen flow before use to insure loss of residual water.

Chemicals

All extraction, nmr, and recrystallization solvents were employed without further purification. "Super-dry" ethanol was prepared by the method of Vogel[388] and benzaldehyde semicarbazone by the method of Shriner, Fuson, and Curtin[389] (procedures detailed herein). Dimethyl sulfoxide (Aldrich) was used as a reaction solvent directly from the manufacturer. All commercial substrates, with the following exceptions, were employed without additional treatment, as were all salts and acidic reagents utilized.

Commercial glutaronitrile (K & K Lab.) was dried over $CaCl_2$ and distilled under vacuum (106°C at 0.6 mm). Practical acrylonitrile (Eastman) was purified after Fieser and Fieser[390]. Substrates that are not designated as commercially available were synthesized by the author (details contained herein). Decolorization of solutions were performed with Nuchar C Carbon Decolorizer (Fisher). Thin-layer chromatography plates were coated with Silica Gel HF 254 (Merck (Germany)). Polyacrylonitrile homopolymer (redox initiated, powder) was supplied by Dr. Gary Wentworth, Chemstrand Research Corp., Durham, North Carolina.

Syntheses of Polyacrylonitrile Models

Preparation of "Super Dry" Ethanol

The "super dry" ethanol was prepared by the method of Vogel[388]. A dry 5-liter,3-neck round bottom flask containing a Teflon-coated stirring bar was fitted with 2 ground-glass stoppers and a Claisen distilling head containing a built-in cold finger and a drying tube filled with anhydrous calcium sulfate. The system was flamed out with a Bunsen burner. After cooling, 10 g (0.41 mole) of clean, dry magnesium turnings (Fisher) and 1.0 g (0.0038 mole) of iodine (Fisher) were placed in the flask, followed by ca. 150 ml of absolute ethanol (Fisher). The mixture was warmed (below reflux) with stirring until the iodine disappeared, accompanied by hydrogen evolution. An additional 1.0 g (0.0038 mole) of iodine was added, and the system heated until the magnesium was converted

into the ethylate. A thick, tan slurry resulted. To this slurry was added 1800 ml of absolute ethanol, and the mixture refluxed overnight (14-16 hr). A forerun of ca. 50 ml was distilled and disregarded, and the remainder of the "super dry" ethanol distilled into a receiver (ca. 1500 ml distillate). The receiver was tightly sealed with a rubber stopper and placed in a desiccator under nitrogen until needed.

Ethyl-2,4-Dicyanopentanoate

The procedure was similar to that reported by Takata and Taniyama[320]. A dry 2-liter, 3-neck round bottom flask containing a Teflon-coated stirring bar was fitted with a condenser topped with a drying tube (anhydrous calcium sulfate), a ground glass stopper, and a 3-neck adaptor. The adaptor was fitted with an internal thermometer and 2 250-ml constant pressure dropping funnels. The system was flamed out with a Bunsen burner, and 500 ml of "super dry" ethanol was added after cooling. With vigorous stirring, 30.6 g (1.33 mole) of "clean" sodium metal (Fisher) was added gradually in small chunks. The sodium ethoxide formation was highly exothermic, and an external ice bath was used to keep the system below reflux. The mixture was stirred until all the sodium had dissolved, and 158.0 g (1.40 mole) of ethyl cyanoacetate (Eastman) was added from 1 of the dropping funnels in a thin stream. The initial clear solution reverted to a thick white paste resembling paint during the addition. The paste was stirred for 10 min, heated to 68°C, the external heat removed,

and 89.5 g (1.33 mole) of methacrylonitrile was added at a slow rate (ca. 14 min) from the remaining dropping funnel. An exothermic reaction took place during the addition, requiring an external ice bath to hold the pot temperature below 75°C. During the addition, the thick paste reverted to a transparent, orange-tint liquid. After addition was complete and the pot temperature had dropped below 70°C (signifying the end of the exotherm), external heat was reapplied and the solution heated at 75°C for 4 hr. The solution was cooled to room temperature, the pot placed in an ice bath, and the solution neutralized (calibrated pH paper) with glacial acetic acid (Fisher). The resulting solid-liquid mixture was transferred to a 2-liter, 1-neck round bottom flask, the ethanol removed by rotary evaporation (aspirator pressure), and 1 liter of distilled water added to the remains. The mixture was extracted with ethyl ether (5 300-ml aliquots), the combined ether extracts dried over anhydrous magnesium sulfate (12 hr), the solution filtered under aspirator suction, the ether removed by rotary evaporation (aspirator pressure), and the opaque red, viscous remains distilled under vacuum. The colorless, viscous ethyl-2,4-dicyanopentanoate (193.1 g, 81%) was collected at 104-110°C (0.2mm) (lit.[320] bp 120°C (1.0 mm); lit.[320] yield 70%). The product exhibited the following characteristics: nmr absorptions at 3.98 (2H, q, $O\underline{CH_2}CH_3$), 3.55 (1H, t, $CH_2\underline{CH}(X)_2$), 2.60 (1H, m, $CH_3\underline{CH}(X)CH_2$), 1.88

(2H, m, CH(X)$\underline{CH_2}$CH(X)$_2$), 1.00 (3H, t, OCH$_2\underline{CH_3}$), 1.00 (3H, d, CH_3CH(X)); major ir absorptions (neat, NaCl plates) located at 2975 (alkane C-H), 2240 (C≡N), 1745 (C=0), 1450 (CH_2), 1375 (CH_3), 1300 (CH), 1270 and 1030 (C-0) cm^{-1}; mass spectra peaks with relative abundances at m/e 180 (parent ion, magnified), 135 (51%), 83 (52%), 80 (44%), 68 (60%), 55 (100%), 45 (35%), 41 (52%), and 29 (92%).

Elemental analysis of $C_9H_{12}N_2O_2$:

Calculated:	C, 59.98; H, 6.71; N, 15.55
Found:	C, 60.06; H, 6.76; N, 15.40
Lit.[320]:	C, 60.06; H, 6.77; N, 15.51

Several modifications of the procedure were attempted. Lower reaction temperatures led to recovery of starting material. Use of 0.23 mole equivalent of base:ethyl cyanoacetate resulted in 19% yield of the monoadduct and 80% yield of the diadduct, 4-carbethoxy-2,4,6-tricyanoheptane (75°C, 2.5 hr). Increase of the NaoEt to 0.65 mole equivalent led to 51% of monoadduct and 38% of the diadduct.

4-Carbethoxy-2,4,6-Tricyanoheptane

The apparatus was the same as for the synthesis of ethyl-2,4-dicyanopentanoate. After assembling and flaming out the apparatus, 450 ml of "super dry" ethanol was added to the pot, followed by 3.17 g (0.14 mole) of "clean" sodium metal chunks (Fisher). After the sodium had dissolved, 110.0 g (0.61 mole) of ethyl-2,4-dicyanopentanoate was added from 1 of

4-carbethoxy-2,4,6-tricyanoheptane that showed the following properties: mp 59-61°C (lit.[320] mp 72-74°C); nmr peaks (C_6H_6, external TMS) at 3.68 (2H, q, $O\underline{CH_2}CH_3$), 2.00 (2H, m, $CH_3\underline{CH}(X)CH_2$), 1.21 (4H, m, $CH(X)\underline{CH_2}C(X)_2$), 0.58 (3H, t, $OCH_2\underline{CH_3}$), and 0.58 (6H, d, $\underline{CH_3}CH(X)$) ppm; ir absorptions (KBr pellet) at 3000 (C-H), 2275 (C≡N), 1750 (C=0), 1450 (CH_2), 1378 (CH_3), 1330 (CH), 1250 and 1025 (C-0) cm^{-1}; and mass spectra major peaks with relative abundances at m/e 247 (parent ion, magnified), 135 (20%), 121 (100%), 68 (26%), 55 (63%), and 29 (60%).

Elemental analysis for $C_{13}H_{17}N_3O_2$:

Calculated:	C, 63.14; H, 6.93; N, 16.99
Found:	C, 63.38; H, 7.02; N, 17.11
Lit.[320]:	C, 63.01; H, 6.88; N, 17.19

In a modified approach, 1 mole equivalent of ethyl cyanoacetate was reacted with 2 mole equivalents of methacrylonitrile, utilizing 0.2 mole equivalents of NaOEt in "super-dry" EtOH (72°C, 2 hr.). The procedure produced a 26% yield of ethyl-2,4-dicyanopentanoate and a 17% yield of 4-carbethoxy-2,4,6-tricyanoheptane.

4-Carboxy-2,4,6-Tricyanoheptane

The procedure was similar in some respects to that reported by Takata and Taniyama[320] and also to that reported by Zahn and Schafer[317] for the conversion of 3-carbethoxy-1,3,5-tricyanopentane to the corresponding carboxylic acid. A 500-ml, 3-neck round bottom flask was equipped with an internal thermometer, a mechanical stirrer, and a condenser. A solution of 14.91 g (0.231 mole pure) of 86.8% potassium hydroxide pellets (Fisher) in absolute EtOH was prepared, allowed to cool to room temperature, and placed in a 60-ml constant pressure dropping funnel. Into the reaction flask were placed 56.49 g (0.228 mole) of 4-carbethoxy-2,4,6-tricyanoheptane and 250 ml of absolute ethanol. The flask was warmed gently with stirring to dissolve the ester, the heat removed, stirring discontinued, and the solution allowed to cool undisturbed to room temperature. The condenser was replaced by the constant pressure dropping funnel containing the potassium hydroxide solution, and the base slowly dropped into the ester solution over a 30 min period. Stirring was begun after the first few drops of solution reached the pot, and an ice bath was used to keep the pot temperature below 25°C during the addition. After *ca.* half of the potassium hydroxide solution had been added, the flow was halted and stirring discontinued. After 1 min of cooling in the ice bath,

the white carboxylic acid salt began to precipitate. Stirring and base addition was resumed, and stirring was continued at a vigorous rate for 10 min after addition was complete to insure total reaction. The acid salt was filtered under aspirator suction, washed with 100 ml of absolute ethanol in 10 ml aliquots, and dried in a vacuum desiccator (1.0 mm) for 24 hr at room temperature. The procedure gave 48.96 g (83.4%) of the white, crystalline potassium salt of 4-carboxy-2,4,6-tricyano-heptane. The 48.96 g of acid salt was dissolved in 43 ml of distilled water contained in a 250-ml erlenmeyer flask. A Teflon-coated stirring bar was added, and the flask positioned in an ice bath at an angle so that the unwetted upper portion of the flask was also cooled. Concentrated commercial hydrochloric acid (Fisher) was cooled in an ice bath and added slowly to the tilted erlenmeyer in individual drops with vigorous stirring. In this manner, each drop of base solution was kept cool by the cold upper flask before reaching the aqueous solution. When the pH reached a level of 2 (calibrated pH paper) addition was halted, and the water layer extracted with 4-175 ml aliquots of ethyl ether. The ether layers were combined over anhydrous sodium sulfate for drying (11 hr), the solution filtered by aspirator suction, and the ether removed by rotary evaporation (aspirator pressure). A viscous, transparent liquid with a slight green tint remained, which

crystallized on standing to give 19.42 g (38.8% based on starting ester, 46.5% based on starting carboxylic acid salt; lit.[320] yield 64% from the ester) of 4-carboxy-2,4,6-tricyanoheptane. The solid was recrystallized from ethyl acetate to give white, crystalline product that exhibited the following properties: mp 114-115°C (lit.[320] mp 130°C); nmr peaks (DMSO-d_6, external TMS) at 10.2 (1H, s, $CO_2\underline{H}$), 2.25 (2H, m, $CH_2\underline{CH}(X)CH_2$), 1.76 (4H, m, $CH(X)\underline{CH_2}C(X)_2$), 0.8 (6H, d, $\underline{CH_3}CH(X)$); ir absorptions (KBr pellet) at 3400 (O-H), 3000 (C-H), 2260 (C≡N), 1750 (C=0), 1450 (CH_2), 1390 (CH_3), 1325 (CH), 1212 and 1030 (C-O), and 900 (O-H) cm^{-1}; mass spectra major peaks with relative abundances at m/e 219 (parent ion, magnified), 176 (30%), 152 (71%), 148 (51%), 121 (100%), 94 (100%), 68 (89%), 55 (73%), 54 (57%), 44 (54%), and 41 (42%).

Elemental analysis for $C_{11}H_{13}N_3O_2$:

Calculated:	C, 60.26; H, 5.98; N, 19.17
Found:	C, 60.14; H, 6.03; N, 19.04
Lit.[320]:	C, 60.21; H, 5.99; N, 19.37

2,4,6-Tricyanoheptane

The decarbalkoxylation procedure of Krapcho and Lovey, who had converted ethyl cyanoacetate to acetonitrile in 85-95% yield, was adapted.[346] A 500-ml, 3-neck round bottom flask was fitted with a condenser topped by a vacuum adaptor with

stopcock, an internal thermometer, and a glass ground stopper. Into the flask were placed in order 200 ml of dimethyl sulfoxide (Aldrich), 72.62 g (0.294 mole) of 4-carbethoxy-2,4,6-tricyanoheptane, 5.71 g (0.0977 mole) of fine sodium chloride particles (Fisher), 11.73 g (0.651 mole) of distilled water, and a Teflon-coated stirring bar. The vacuum adaptor was connected by Tygon and glass tubing to a saturated, aqueous barium hydroxide solution functioning as a gas trap, and rapid heating (mantel) with vigorous stirring was begun. Carbon dioxide evolution was observed via insoluble barium carbonate formation in the gas trap at 150°C. The pot temperature leveled at 150-152°C, and was held at that temperature. After 10 min, the trap became plugged, necessitating removal of the vacuum adaptor. Periodically, the gas trap was recharged with fresh, saturated barium hydroxide solution and reattached to the condenser to monitor the carbon monoxide evolution. After 2½ hr, no barium carbonate formation could be observed, and the system was cooled after removal of the vacuum adaptor. The DMSO solution was poured into 800 ml of distilled water, and extracted with 3-225 ml aliquots of chloroform. The solvent was removed by rotary evaporation (aspirator pressure), the remains placed in 500 ml of distilled water, and the aqueous solution extracted with 4-150 ml aliquots of chloroform. The combined chloroform extracts were placed over anhydrous magnesium sulfate for drying (8 hr), and the salt filtered by aspirator suction to give (after removal

of the solvent by rotary evaporation (aspirator pressure)) 50.20 g of a yellow tint, transparent viscous liquid. Distillation yielded initially a low-boiling forerun of 9.73 g (31%) of 1,3-dicyanobutane as a clear, colorless liquid, bp 76-80°C (0.15 mm). Analysis was the same as for 1,3-dicyanobutane synthesized directly by decarbalkoxylation of ethyl-2,4-dicyanopentanoate (described herein). Continued distillation yielded 30.68 g (60%; lit.[320] yield by alternate, multi-step method, 54%) of 2,4,6-tricyanoheptane, bp 156-160°C (0.10 mm) (lit.[320] bp 212-4°C at 10 mm), as a yellow tint, viscous liquid. The liquid crystallized to a wax-like, semi-crystalline solid on sitting for several weeks: mp (DTA, N_2 atmosphere, 8°C/min) 55°C; nmr peaks ($CDCl_3$, external TMS) at 3.00 (3H, m, $CH_3\underline{CH}(X)CH_2$, $CH_2\underline{CH}(X)CH_2$), 2.00 (4H, $CH(X)\text{-}\underline{CH_2}CH(X)$), 1.47 (6H, d, $\underline{CH_3}CH(X)$); ir absorptions (film, NaCl plates) at 3575 (weak, H_2O or NH impurity), 2925 (C-H), 2230 (C≡N), 1625 (weak, H_2O or C=N impurity), 1450 (CH_2), 1375 (CH_3), 1340 (CH) cm^{-1}; mass spectra peaks with relative abundances at m/e 175 (parent ion, 2%), 121 (93%), 94 (41%), 68 (100%), 54 (85%), and 41 (58%); ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) with per cent heights at 121.585 (34%) and 121.285 (56%) ($CH_3CH(\underline{C}N)CH_2$); 119.464 (50%, $CH_2CH(\underline{C}N)CH_2$); 36.038 (34%, 2 coalesced peaks), 35.492 (22%), and 34.946 (19%) ($CH_2\underline{C}H(CN)CH_2$); 28.940 (15%), 28.091 (20%), and 26.998 (10%) ($CH(CN)\underline{C}H_2CH(CN)$); 24.147 (42%) and 23.237 (33%) ($CH_3\underline{C}H(CN)CH_2$); 18.019 (42%) and 17.412 (29%)

($\underline{CH}_3CH(CN)$) ppm. The ir spectra (except for less-prominent impurity peaks) corresponded to that of Takata and Taniyama[320], and the ^{1}H-nmr spectra to that of Murano and Yamadera[327].

Elemental analysis of $C_{10}H_{13}N_3$:

Calculated:	C, 68.54; H, 7.48
Found:	C, 68.52; H, 7.48
Lit.[320]:	C, 68.46; H, 7.16

Thus only the ir analysis detected the (insignificant) impurities.

1,3-Dicyanobutane

The apparatus and procedure was the same as for the synthesis of 2,4,6-tricyanoheptane. Into the reaction flask were placed in order 135 ml of dimethyl sulfoxide (Aldrich), 35.80 g (0.199 mole) of ethyl-2,4-dicyanopentanoate, 7.99 g (0.137 mole) of fine particles of sodium chloride, and 8.13 g (0.451 mole) of distilled water. Reaction time was 2 hr. The DMSO solution was placed in 1-liter of distilled water, and extracted with 4-225 ml aliquots of chloroform. The combined chloroform extracts were placed over anhydrous magnesium sulfate for drying (12 hr), the salt filtered by aspirator suction, and the chloroform removed by rotary evaporation (aspirator pressure). Distillation of the remains produced a forerun of residual DMSO (96-100^{o}C at 10 mm)

followed by 18.68 g (87%) of 1,3-dicyanobutane collected as a clear, colorless liquid: bp 72-75°C (0.05 mm); nmr peaks (neat, external TMS) at 2.50 (3H, m, $CH_3\underline{CH}(X)CH_2$ and $CH_2\underline{CH_2}$-(X)), 1.85 (2H, m, $CH(X)\underline{CH_2}CH_2(X)$), 1.17 (3H, d, $\underline{CH_3}CH(X)$) ppm; ir absorptions (neat, NaCl plates) at 2975 (C-H), 2250 (C≡N), 1435 (CH_2), 1385 (CH_3) cm^{-1}; mass spectra peaks with relative abundances at m/e 108 (parent ion, 5%), 80 (44%), 68 (70%), 66 (44%), 55 (62%), 41 (72%), 28 (100%), and 27 (54%); ^{13}C-nmr ($CDCl_3$, internal TMS, proton decoupled) with per cent heights at 121.468 (67%, $CH\underline{C}N$), 118.551 (73%, $CH_2\underline{C}N$), 29.365 (55%, $\underline{C}H_2$), 24.693 (76%, $\underline{C}HCN$), 17.352 (46%, $\underline{C}H_3$), and 15.107 (47%, $\underline{C}H_2CN$) ppm.

4,6-Dicarbethoxy-2,4,6,8-Tetracyanononane (Crude)

The method was patterned after that of Takata and Taniyama[320]. A bomb was prepared by threading a 2-in inside diameter steel tube on both ends, permanently capping one end, and drilling ¼-in holes just below the threads of the other end. A 3-neck, 500-ml round bottom flask containing a Teflon-coated stirring bar was fitted with a condenser topped by a drying tube (anhydrous calcium sulfate) and 2 glass-ground stoppers. Into the flask were placed 135 ml of "super-dry" ethanol followed by 8.06 g (0.35 mole) of "clean" sodium metal chunks. After the sodium had dissolved, 53.40 g (0.296 mole) of ethyl-2,4-dicyanopentanoate was added to the pot with stirring in 10 g aliquots, the solution stirred for 10 min, and the pot

placed in an ice bath for cooling. From a 60-ml constant pressure dropping funnel, 26.20 g (0.15 mole) of dibromomethane (methylene bromide, Eastman) was added in a slow stream to the cold solution. After stirring for 10 min, the cold mixture was transferred to a long-necked, heavy-walled glass tube (¼-in thickness, 1 3/4-in outside diameter) and the tube was sealed by the method of Bates[391]. The contents of the tube were frozen in an ice-acetone bath, the acetone wiped off, and a glass rod fused to the top of the tube neck using an oxygen torch. The neck was heated just below the top and slowly drawn until the separation was complete. The bubble at the top of the sealed neck was annealed to insure tight closure, the tube was placed in the steel bomb, and sand filled in around the tube to enhance heat conduction. The bomb was capped (hand tightness) and placed in a silicon oil (Arthur H. Thomas Co.) constant temperature bath held at 90°C by a Thermo-Watch Constant Temperature Control (Fisher). The temperature was held for 5 hr, the tube allowed to cool for ca. 12 hr, and then opened by the method of Bates[391]. The tube contents were frozen in a dry ice-acetone bath, the acetone wiped off, and the torch flame concentrated on a point ca. 1-in below the seal of the tube neck until the soft glass bubbled inward (indicating no excess pressure). The neck was then scratched circularly with a glass cutter, the scratch wetted and heated with the torch (below the softening point of the glass), and the top removed by tapping lightly.

The remaining base was neutralized with glacial acetic acid (calibrated pH paper), the red, solid-liquid mixture placed in 1000 ml of distilled water, and the water layer extracted with 5-250 ml aliquots of ethyl acetate. The combined ethyl acetate extracts were dried over anhydrous magnesium sulfate (10 hr), the drying agent filtered by aspirator suction, and the ethyl acetate removed by rotary evaporation (aspirator pressure) followed by vacuum desiccation (10 hr, 1.2 mm). A total of 49.58 g (90%; lit.[320] yield 75%) of crude 4,6-dicarbethoxy-2,4,6,8-tetracyanononane was obtained as a viscous, opaque red liquid. The crude material was undistillable[320] due to the high molecular weight, and thin layer chromatography (silica gel, variety of solvents and mixtures) of the multi-polar polyacrylonitrile models and their ester analogs showed that the desired compounds were inseparable from the polar by-products via chromatography. Therefore, the crude 4,6-dicarbethoxy-2,4,6,8-tetracyanononane was used in the following steps. Analysis of the crude diester exhibited the following: nmr peaks ($CHCl_3$, external TMS) at 4.40 (4H, q, $O\underline{CH_2}CH_3$), 3.00 (2H, m, $CH_3\underline{CH}(X)CH_2$), 2.10 (6H, m, $CH(X)\underline{CH_2}$-$C(X)_2$ and $C(X)_2\underline{CH_2}C(X)_2$), 1.45 (6H, t, $OCH_2\underline{CH_3}$), and 1.45 (6H, d, $CH(X)\underline{CH_3}$) ppm; ir absorptions (neat, NaCl plates) at 2975 (C-H), 2255 (C≡N), 1755 (C=O), 1450 (CH_2), 1378 (CH_3), 1305 (CH), 1270 and 1030 (C-O) cm^{-1}; mass spectra major peaks with relative abundances at m/e 174 (5%), 135 (9%), 121 (100%), 94 (12%), 84 (21%), 68 (14%), 55 (55%), 45 (12%), 41 (12%), 29 (61%) and 27 (36%).

4,6-Dicarboxy-2,4,6,8-Tetracyanononane (Crude)

The procedure was patterned after that of Takata and Taniyama.[320] A 3-neck, 1-liter round bottom flask containing a Teflon-coated stirring bar was fitted with a condenser, a 500-ml constant pressure dropping funnel, and a glass-ground stopper. Into the flask was placed 200 ml of absolute ethanol (Fisher) and 50.18 g (0.135 mole) of crude 4,6-dicarbethoxy-2,4,6,8-tetracyanononane. After stirring for 5 min, an ice bath was used to cool the pot, and a solution of 18.10 g (0.323 mole pure) of 87.8% potassium hydroxide pellets (Fisher) in 250 ml of absolute ethanol was dropped in from the constant pressure funnel over a 20 min period. The system was stirred for 7 hr, stirring was discontinued, and the system allowed to sit for 8 hr. The potassium salt of the dicarboxylic acid was precipitated, filtered by suction, and washed with five 50 ml aliquots of absolute ethanol. After drying under vacuum (12 hr, 1.0 mm), 41.04 g (77%; lit.[320] yield 76%) of the potassium salt of 4,6-dicarboxy-2,4,6,8-tetracyanononane were isolated as a light tan solid. Into a 50-ml erlenmeyer flask were placed 5.0 ml of concentrated commercial (36-37%) hydrochloric acid (Fisher) and a small Teflon-coated stirring bar. The bottom of the erlenmeyer was submerged in an ice bath, vigorous stirring begun, and 15.0 g (0.038 mole) of the potassium salt of 4,6-dicarboxy-2,4,6,8-tetracyanononane were added over a 30 min period. When the pH reached a level of 2 (calibrated pH paper), the mixture was washed into a 250-ml erlenmeyer with

150 ml of ethyl acetate. An orange liquid and white potassium chloride salt separated, the salt was filtered by aspirator suction, and the solid washed with 5-10 ml aliquots of ethyl acetate. The solution was dried over anhydrous magnesium sulfate (9 hr), the drying agent filtered, and the ethyl acetate removed by rotary evaporation (aspirator pressure) followed by vacuum desiccation (10 hr at 1.3 mm). The crude product was obtained as 10.52 g (87% based on the potassium salt (lit.[320] yield 91%); 67% based on the diester (lit.[320] yield 69%)) of a glass-like material that crystallized to a white, wax-like solid on sitting for several days. Analysis of the crude 4,6-dicarboxy-2,4,6,8-tetracyanononane (used in the following step) yielded: nmr peaks (DMSO-d_6, external TMS) at 4.18 (2H, s, COO<u>H</u>), 1.38 (2H, m, $CH_3\underline{CH}(X)CH_2$), 1.05 (6H, m, $CH(X)\underline{CH_2}C(X)_2$ and $C(X)_2\underline{CH_2}C(X)_2$), and 0.6 (6H, d, $\underline{CH_3}CH(X)$) ppm; ir absorptions (film, NaCl plates) at 3400 (O-H), 2950 (C-H), 2250 (C≡N), 1725 (C=O), 1465 (CH_2), 1375 (CH_3), 1225 and 1025 (C-O), and 925 (O-H) cm^{-1}.

<u>2,4,6,8-Tetracyanononane, Method I (Crude)</u>

The method was similar to that of Takata and Taniyama[320]. Into a 100 ml round bottom flask were placed 5.01 g (0.0158 mole) of crude 4,6-dicarboxy-2,4,6,8-tetracyanononane and 5.00 g (0.0788 mole) of copper metal dust (Fisher). The 2 were mixed well and a vacuum adaptor with stopcock was fitted to the flask. The adaptor was connected to a vacuum line, a pressure of 0.5 mm obtained, and the flask submerged

in an oil bath held at 200°C (Thermo-Watch Constant Temperature Control (Fisher)) for 4 min. The pressure increased to 3.4 mm during the period, and then decreased back to 0.5 mm. While the reaction mixture was still hot, a Teflon-coated stirring bar was added along with 50 ml of warm toluene (Fisher). The solution was stirred for several minutes, poured into a separate flask, and the toluene treatment of the residue repeated with 4-50 ml aliquots. The combined toluene washings were filtered several times under aspirator suction to remove the copper, and the yellow tint removed by carbon decoloration. The toluene solution was placed in a 500-ml erlenmeyer flask, 1.0 g of Nuchar C Carbon Decolorizer (Fisher) was added along with a Teflon-coated stirring bar, and the mixture heated slowly to reflux with stirring in a hood. After refluxing for 10 min, the carbon was removed by filtration through a sintered glass funnel under aspirator suction to yield a clear solution. The toluene was removed by rotary evaporation (aspirator pressure) to give 0.482 g (13% based on diacid (lit.[320] yield 50%); 0.9% based on diester (lit.[320] yield 34%)) of 2,4,6,8-tetracyanononane as a wax-like, milky-white solid. Analysis gave the following results: nmr peaks (C_6H_6, external TMS) at 2.05 (4H, m, $CH_3\underline{CH}(X)CH_2$), 0.9 (6H, m, $CH(X)\underline{CH_2}CH(X)$), 0.5 (6H, d, $\underline{CH_3}CH(X)$); ir absorptions (film, NaCl plates) at 3500 and 3400 (O-H and N-H impurity), 3000 (C-H), 2275 (C≡N), 1700 (several overlapping peaks, C=O impurities), 1616 (C=N impurity),

1460 (CH_2), 1385 (CH_3), 1220 and 1060 (C-O impurity) cm^{-1}; mass spectra major peaks with relative abundances at m/e 212 (30%, impurity), 195 (25%, impurity), 167 (30%, impurity), 121 (28%), 92 (100%), 68 (22%), 55 (33%), 40 (17%), and 27 (15%).

Elemental analysis for $C_{13}H_{16}N_4$:

Calculated: C, 68.39; H, 7.06

Found: C, 65.50; H, 6.97

Lit.[320]: C, 67.96; H, 7.01

The overall analysis thus showed that impurities, probably of the $CONH_2$, COOH, and C=N types, were present. The ir spectra (including the impurity peaks) corresponded to that of Takata and Taniyama[320].

2,4,6,8-Tetracyanononane, Method II (Crude)

The method and apparatus, except for the employment of a 250-ml reaction flask, was the same as in the synthesis of 2,4,6-tricyanoheptane. Into the flask were placed in order 90 ml of dimethyl sulfoxide (Aldrich), 25.28 g (0.068 mole) of crude 4,6-dicarbethoxy-2,4,6,8-tetracyanononane, 2.61 g (0.037 mole) of fine sodium chloride particles (Fisher), 5.27 g (0.293 mole) of distilled water, and a Teflon-coated stirring bar. Carbon dioxide evolution began at 149°C, the pot temperature leveled at 154°C, and was held at that temperature for 2½ hr. The bulk of the DMSO was separated by vacuum distillation (bp 35°C at 0.2 mm), the remains placed in 600 ml of

distilled water, and the water layer extracted with 3-200 ml portions of chloroform (Fisher). The combined chloroform extracts were placed over anhydrous magnesium sulfate for drying (5 hr), the drying agent filtered by aspirator suction, and the chloroform removed by rotary evaporation (aspirator pressure). The extraction procedure was repeated, followed by vacuum desiccation (3 hr, 0.1 mm) to remove the residual chloroform. A total of 13.8 g (89%) of crude 2,4,6,8-tetracyanononane was obtained as an opaque black, viscous liquid, with analysis as follows: nmr peaks ($CHCl_3$, external TMS) at 2.95 (4H, m, $CH_n\underline{CH}(X)CH_2$, n=2-3), 2.10 (6H, m, $CH(X)\underline{CH_2}CH(X)$), 1.40 (6H, d, $\underline{CH_3}CH(X)$) ppm; and ir absorptions at 3400 (O-H or N-H impurity), 2950 (C-H), 2240 (C≡N), 1700 (C=O impurity, 1625 (C=N impurity), 1460 (CH_2), 1385 (CH_3), 1235 and 1050 (C-O impurity) cm^{-1}. Attempted purification by carbon decolorization failed to eliminate the impurities and color, though the treated material did partially crystallize to the characteristic wax-like solid on sitting for several weeks. A type of liquid-to-solid distillation was successful on a small scale as follows: In the well of a small sublimation apparatus with built-in cold finger, vacuum adaptor, and solvent reflux path was placed crude 2,4,6,8-tetracyanononane. Ice water was circulated through the cold finger, xylene (bp 138-141^{o}C) was used as the reflux solvent, and a pressure of 0.1 mm was attained. A mixture of wax-like solid and a viscous, yellow-tint liquid formed on the cold

finger over a period of 7 hr. Nmr spectra was the same as for the crude material. The ir absorptions were also the same, indicating that the chemical impurities were not eliminated by the process. Large-scale attempts of this method failed due to excessive splattering of the viscous material upon heating. Column chromatography and normal distillation were not considered due to the reasons given for possible purification techniques for 4,6-dicarbethoxy-2,4,6,8-tetracyanononane. The ir spectra of the crude product overlapped with that synthesized by the Takata and Taniyama method.

3-Carbethoxy-1,3,5-Tricyanopentane, Method I

Commercial acrylonitrile was purified by the method of Fieser and Fieser[390]. Utilizing a 2-liter separatory funnel, 1500 ml of practical grade acrylonitrile (Eastman) were washed in succession with 300 ml portions of 10% sulfuric acid, 10% sodium carbonate, and saturated sodium sulfate solutions. The acrylonitrile was distilled at atmospheric pressure (by 78-80°C) utilizing a Vigreux column, and then redistilled under high vacuum (1.0 mm) with low heat and a dry ice-acetone cooled receiver. The synthetic procedure for the ester precursor of the model was patterned after that of Zahn and Schafer[317], who in turn had utilized the observations of earlier workers in formulating their method[311-314]. A solution of methanolic potassium hydroxide was prepared by dissolving 1.22 g (0.019 mole pure) of 87.8% potassium hydroxide pellets

(Fisher) in 4.5 ml of methanol (Fisher). A 3-neck, 1-liter round bottom flask was fitted with a mechanical stirrer, an internal thermometer, and a ground glass stopper. Into the flask were poured 100 g of 1,4-dioxane (Fisher) and 56.31 g (0.498 mole) of ethyl cyanoacetate (Eastman). The mixture was stirred thoroughly, and the glass-ground stopper replaced by a 2-neck adaptor containing a calibrated 25-ml constant pressure dropping funnel and a 60-ml constant pressure dropping funnel. Approximately 1.5 ml of the prepared potassium hydroxide solution were added to the flask from the 25-ml funnel, the solution stirred for 5 min, and 53.09 g (1.00 mole) of purified acrylonitrile added dropwise from the 60-ml dropping funnel with vigorous stirring. An exothermic reaction occurred, and an ice bath was used to hold the solution temperature below 40°C. After the initial stages of the reaction, 1 ml aliquots of the methanolic potassium hydroxide solution was added dropwise at intervals to insure a presence of base (3.5 ml total base solution added, ca. 0.95 g (0.015 mole) of 87.8% potassium hydroxide). After the exotherm dissipated, the solution was stirred vigorously for 2 hr at room temperature and then neutralized with 2N hydrochloric acid. The dioxane solution was placed in 1 liter of distilled water, the aqueous solution extracted with 5-250 ml aliquots of ethyl acetate, and the combined extracts placed over anhydrous sodium sulfate (5 hr) for drying. The salt was filtered by aspirator suction, and the ethyl acetate and residual dioxane were

removed by rotary evaporation (aspirator pressure) followed by vacuum desiccation (12 hr at 1.0 mm). An opaque brown, viscous liquid resulted which solidified on cooling under vacuum (-10°C at 1.0 mm) to give 102.84 g (94%; lit.[317] yield 97%) of crystalline (spherulytic), colored 3-carbethoxy-1,3,5-tricyanopentane. Distillation failed due to excessive tarring before the bp was reached (194-6°C at 0.1 mm). Zahn and Schafer[317] and Bruson and Reiner[312] had reported purification by recrystallization from ethanol. However, ethanol appeared to be a poor choice for the low-melting (35-35.5°C (crystalline)) ester. Oil formation occurred from the saturated, hot solutions on cooling in preference to recrystallization. Practically all of the solvent had to be air evaporated before recrystallization was initiated. A variety of common solvents and their mixtures were tested as recrystallization media without success. A new purification procedure based on a type of liquid-to-solid distillation was thus developed: In the well of a 4-in diameter sublimation apparatus with built-in cold finger, vacuum adaptor, and solvent reflux path was placed crude, crystalline 3-carbethoxy-1,3,5-tricyanopentane. Ice water was circulated through the cold finger, xylene (bp 138-141°C) was used as the reflux solvent, and a pressure of 0.05-0.10 mm was maintained. After 4 hr, a thick layer of white, wax-like solid had formed on the cold finger. The process was halted, the solid removed, and the procedure repeated until only a tar-like, colored film remained in the sublimator

well. The wax-like solid was found to form spherulytic crystals upon dissolving in organic solvents followed by evaporation of the solvent in air. Analysis of the purified 3-carbethoxy-1,3,5-tricyanopentane gave the following results: mp ("sublimed" product) 33.2-33.7°C; mp ("sublimed" product after crystallization from solvent) 35-35.5°C (lit.[317] mp 37°C); nmr peaks (C_6H_6, external TMS) at 3.50 (2H, q, $O\underline{CH_2}CH_3$), 1.42 (4H, m, $CH_2(X)\underline{CH_2}$) ppm; ir absorptions (film, NaCl plates) at 2980 (C-H), 2250 (C≡N), 1735 (C=O), 1450 (CH_2), 1375 (CH_3), 1250 and 1018 (C-O) cm^{-1}; mass spectra peaks with relative abundances at m/e 219 (parent ion, 4%), 193 (36%), 175 (63%), 149 (54%), 136 (76%), 120 (54%), 109 (79%), 93 (51%), 81 (91%), 54 (65%), 41 (34%), and 29 (100%).

Elemental analysis for $C_{11}H_{13}N_3O_2$:

Calculated:	C, 60.25; H, 5.98; N, 19.17
Found:	C, 60.10; H, 6.03; N, 19.22
Lit.[317]:	C, 60.60; H, 6.00; N, 19.29

3-Carbethoxy-1,3,5-Tricyanopentane, Method II

The procedure was derived as a result of the discoveries made in the attempted synthesis of ethyl-2,4-dicyanobutanoate (detailed herein). A dry, 3-neck, 1-liter round bottom flask containing a large Teflon-coated stirring bar was equipped with a condenser topped by a drying tube (anhydrous calcium chloride), a glass-ground stopper, and a

2-neck adaptor fitted with 2-250-ml constant pressure dropping funnels. The flask was charged with 400 ml of "super-dry" ethanol and 4.93 g (0.214 mole) of "clean" sodium metal chunks. After the sodium had dissolved, 90.85 g (0.803 mole) of ethyl cyanoacetate (Eastman) were added with stirring from one of the dropping funnels over a 10 min period. After the addition was complete, the stopper was replaced with an internal thermometer, and the solution was cooled to -10°C by submerging the flask in an ice-acetone bath. After cooling and stirring for 10 min, 85.77 g (1.62 mole) of purified acrylonitrile was added slowly with vigorous stirring from the remaining dropping funnel (2 hr) while the temperature was not allowed to rise above +10°C. After addition was complete and the exotherm had dissipated, the solution temperature was equilibrated at 0°C and held at that temperature with stirring for 1 hr. The cold ethanolic solution was neutralized with 2N hydrochloric acid (calibrated pH paper), the solvent removed by rotary evaporation (aspirator pressure), and the remains placed in 1 liter of distilled water. The aqueous solution was extracted with 4-250 ml aliquots of ethyl acetate, the extracts combined over anhydrous magnesium sulfate for drying (5 hr), the salt filtered by aspirator suction, and the ethyl acetate removed by rotary evaporation (aspirator pressure). A viscous, yellow tint, transparent liquid was obtained. Partial distillation was performed to remove the residual ethyl cyanoacetate (bp 35-40°C at 0.1 mm; 3.93 g recovered (4.3% of starting

material)); nmr peaks (neat, internal TMS) at 4.25 (2H, q, $O\underline{CH_2}CH_3$), 3.60 (2H, s, $\underline{CH_2}(X)C(X)_2$), and 1.30 (3H, t, $OCH_2\underline{CH_3}$) ppm. After the ethyl cyanoacetate had been removed, distillation was discontinued, and the remains solidified upon cooling under vacuum (-10°C, 1.0 mm) to yield 138.8 g (79% based on starting material; 82.5% based on recovered ethyl cyanoacetate) of spherulytic crystalline 3-carbethoxy-1,3,5-tricyanopentane possessing a slight yellow tint. The product was sufficiently pure for use in subsequent syntheses, with analyses corresponding to that of the purified 3-carbethoxy-1,3,5-tricyanopentane in Method I. The slight coloration was removable via the liquid-to-solid distillation technique detailed in Method I.

1,3,5-Tricyanopentane, Method I

The apparatus and procedure was the same as for the synthesis of 2,4,6-tricyanoheptane. Into the reaction flask were placed in order 100 ml of dimethyl sulfoxide (Aldrich), 20.11 g (0.092 mole) of 3-carbethoxy-1,3,5-tricyanopentane, 1.93 g (0.033 mole) of fine sodium chloride particles (Fisher), and 5.37 g (0.30 mole) of distilled water. Carbon dioxide began evolving at 152°C, the pot temperature stabilized at 168-170°C, and the system was held at that temperature until no further gas evolution was observed (2½ hr). The DMSO solution was placed in 800 ml of distilled water, the water layer extracted with 4-250 ml aliquots of chloroform, and the combined extracts placed over anhydrous magnesium sulfate for drying (5 hr). The salt was filtered by aspirator suction and

the chloroform removed by rotary evaporation to give 13.40 g of an orange tint, transparent liquid. Distillation gave low-boiling fractions of residual DMSO (bp 35-37°C at 0.08 mm; nmr (neat, external TMS) singlet at 2.45 ppm)), and 0.84 g (10%) of 1,3-dicyanopropane (glutaronitrile): bp 85-87°C at 0.18 mm; nmr peaks (neat, external TMS) at 2.50 (4H, t, $\underline{CH_2}(X)CH_2$) and 1.85 (2H, m, $CH_2(X)\underline{CH_2}$). The boiling range and nmr analysis coincided with that of commercial 1,3-dicyanopropane (K & K Lab.). Continued distillation yielded 6.97 g (52%; lit.[317] yield by alternate, multistep method, 34%) of 1,3,5-tricyanopentane as a viscous, yellow tint liquid (the remainder of the distillation pot material tarred): bp 185-187°C at 0.08 mm (lit.[317] bp 85°C at less than 0.01 mm (repeated short distillations)); nmr peaks ($CDCl_3$, external TMS) at 3.00 (1H, m, $CH_2\underline{CH}(X)CH_2$), 2.70 (4H, t, $\underline{CH_2}(X)CH_2$), and 2.05 (4H, m, $CH_2(X)\underline{CH_2}CH(X)$) ppm; ir absorptions (neat, NaCl plates) at 3600 (N-H impurity), 2912 (C-H), 2245 (C≡N), 1650 (C=N impurity), 1435 (CH_2), and 1350 (C-H) cm^{-1}; mass spectral peaks with relative abundances at m/e 147 (parent ion, magnified), 93 (3%), 78 (100%), 63 (100%), 58 (71%), 54 (40%), 43 (96%), 41 (41%) and 28 (44%); ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) with per cent heights at 119.279 (36%, $CH(\underline{C}N)$), 118.493 (81%, $CH_2(\underline{C}N)$), 29.910 (30%, $\underline{C}H(CN)$), 27.241 (39%, $\underline{C}H_2$), and 15.167 (40%, $\underline{C}H_2(CN)$) ppm; ^{13}C-nmr peaks ($CDCl_3$, internal TMS, off-resonance (weak proton coupling)) at 119.279 (s, $CH(\underline{C}N)$),

118.493 (s, $CH_2(\underline{C}N)$), 29.910 (d, $\underline{C}H(CN)$), 27.241 (t, $\underline{C}H_2$), and 15.167 (t, $\underline{C}H_2CN$).

Elemental analysis for $C_8H_9N_3$:

Calculated:	C, 65.28; H, 6.16
Found:	C, 65.01; H, 6.21
Lit.[317]:	C, 65.02; H, 6.17

Thus the minor impurities present were detectable only by ir analysis.

1,3,5-Tricyanopentane, Method II

Studies showed that for several reactive esters, sodium chloride was not necessary to effect decarbalkoxylation in the adapted Kapcho-Lovey method[346] (details contained herein). Thus the procedure for Method II, synthesis of 1,3,5-tricyanopentane, was the same as Method I but without use of sodium chloride. Into the reaction flask were placed 20.30 g (0.093 mole) of 3-carbethoxy-1,3,5-tricyanopentane, 3.78 g (0.21 mole) of distilled water, and 100 ml of dimethyl sulfoxide (Aldrich). Carbon dioxide began evolving at 168°C, the refluxing ethanol-water mixture removed (bp 78-98°C) by opening the distillation head stopcock until the pot temperature reached 175°C, and the system held at that temperature by periodically distilling the ethanol as it was formed. After 4.7 hr, the amount of carbon dioxide evolution was negligible, and the system was cooled. Work-up was the same as in Method I, except that a

second washing-extraction procedure was conducted. The chloroform was removed from the final extracts after drying to give 11.81 g of an orange tint, transparent liquid. Distillation gave 2.58 g (30%) of 1,3-dicyanopropane (bp 75-78°C at 0.05 mm) and a fraction consisting (by nmr analysis) a mixture of 1,3,5-tricyanopentane and 3-carbethoxy-1,3,5-tricyanopentane (bp 183-190°C at 0.05 mm). The presence of the ester was revealed by nmr peaks ($CHCl_3$, external TMS) at 4.40 (q, $O\underline{CH_2}CH_3$) and 1.40 (t, $OCH_2\underline{CH_3}$) ppm. Nmr integration analysis showed the mixture to consist of 1.62 g (8%) of the starting ester and 4.30 g (32% based on starting ester; 34% based on recovered starting material) of 1,3,5-tricyanopentane.

Attempted Preparation of Ethyl-2,4-Dicyanobutanoate

The apparatus and sequence of reagent addition was the same as in the preparation of 3-carbethoxy-1,3,5-tricyanopentane, Method II. Into the flask were placed 400 ml of "super-dry" ethanol followed by 4.63 g (0.201 mole) of "clean" sodium metal chunks. After the sodium had dissolved, 125.3 g (1.13 mole) of ethyl cyanoacetate (Eastman) was dropped in with stirring over a 10 min period, the solution cooled to -43°C by submerging the flask in a dry ice-acetone bath, and 43.05 g (0.81 mole) of purified acrylonitrile (Eastman) was added at a rate designed to hold the solution temperature below -38°C (ca. 30 min). After addition was complete, the solution was stirred for 30 min at -40°C, and then neutralized (cold) with 2N hydrochloric acid (calibrated pH paper). The solvent was

removed by rotary evaporation (aspirator pressure), the remains placed in 500 ml of distilled water, and the aqueous solution extracted with 4-275 ml aliquots of ethyl ether. The ether extracts were combined over anhydrous sodium sulfate for drying (5 hr), the salt filtered (suction), and the solvent removed by rotary evaporation (aspirator pressure). Distillation gave 87.8 g (70% of starting material) of ethyl cyanoacetate (bp 51-53°C at 0.1 mm) and 24.8 g (28% based on acrylonitrile) of 3-carbethoxy-1,3,5-tricyanopentane (bp 194-196°C at 0.1 mm). No ethyl-2,4-dicyanobutanoate was detected. The dialkylated product crystallized in the cold under vacuum (-10°C at 1.2 mm) to white spherulytic crystals. Physical methods confirmed the identities of the 2 fractions (see the synthesis of 3-carbethoxy-1,3,5-tricyanopentane, Methods I and II, for analyses).

DTA/TGA Analyses of PAN and its Models

Procedure

Differential thermal analyses/thermogravimetric analyses (DTA/TGA) were performed for the 2 pure 3-unit models of polyacrylonitrile (1,3,5-tricyanopentane (18) and 2,4,6-tricyanoheptane (19), both prepared by the DMSO method), the impure 4-unit model of polyacrylonitrile (2,4,6,8-tetracyanononane (20), prepared by the Takata and Taniyama[320] method), and polyacrylonitrile (PAN) homopolymer (redox initiated). A Mettler Thermoanalyzer II instrument plotted simultaneously the actual weight loss and weight loss-times-ten (TGA) curves,

DTA curves, and temperature curves. Standard conditions employed were sample sizes of 30-80 mg, the use of dry aluminum oxide as a standard, and the use of macro-size platinum crucibles. The atmosphere under which the experiments were conducted was either dry air or dry nitrogen, and a heating rate of 2°C, 4°C, or 8°C/min was used. For the dry air runs, an air filter containing anhydrous calcium sulfate was placed between a small air pump and the air-intake valve of the instrument in order to supply the system with a steady flow of dry air. The nitrogen employed was obtained dry from the manufacturer. The Thermoanalyzer was set up according to manufacturer's instructions (see the Instrumentation and Apparatus section for constant instrument settings). The platinum crucibles were heated at 900°C for a minimum of 3 hr in a ceramic furnace to insure complete pyrollization and removal of organic material and to redry the aluminum oxide standard before each experiment.

To begin a test, the platinum crucibles were removed from the oven, cooled, weighed, and dry aluminum oxide weighed into one of the crucibles designated as the reference (250-300 mg when aluminum oxide was employed in the other (sample crucible), and an equivalent amount to the sample weight when aluminum oxide was not used with the sample. In most of the tests, aluminum oxide was mixed with the compound tested in the sample crucible (weight of solid in the reference crucible less the weight of sample used).

In the remainder of the examinations, aluminum oxide was omitted from the sample crucible in order to assess any catalytic effect on the degradation of PAN or its models. The material to be tested was weighed into the sample crucible, mixed well with the aluminum oxide (where required), and the 2 crucibles placed on the proper posts of the ceramic thermocouple unit. The machine was calibrated to the relative weights of the 2 crucibles, the furnace placed around the crucible holder, and the gas flow regulated to 6 lb/hr *via* a valve placed in the gas line. After running the recorder several minutes to insure equilibration, heating was begun and the graphs plotted automatically over a period of several hours. After shutdown and cooling of the furnace, the crucibles were placed in the ceramic oven in preparation of the next experiment.

The critical data recorded from the DTA graphs were the temperatures at which major exothermic and endothermic (where applicable) transitions began and/or the temperature at which the standard and sample crucibles reached a state of maximum conductivity difference (denoted by a peak). The temperatures were found by projecting the concerned point of the DTA (or TGA) curve to the plotted temperature curve, and projecting that point in turn to a linear temperature scale transferred onto the graph paper. Complete or near-complete sample weight loss was indicated by a levelling of the TGA curve. From the TGA curves, the total per cent weight losses

at the major DTA transitions or any temperature point were determined by assigning the initial weight of the sample to the level portion of the plot at 25°C and dividing that quantity into the weight loss for the concerned region. As the paper was calibrated in 1 mg units, the actual weight loss for any region was read directly from the graph by the number of units that the TGA curve had traversed from the initial reading at 25°C to the point in question.

Analyses of Polyacrylonitrile

Dry Air Tests. At a heating rate of 8°C/min and with aluminum oxide mixed with the polymer (52.5 mg sample weight), a strong, sharp exotherm began at 210°C, peaked at 295°C, and the associated weight loss ended at 308°C (34% total weight loss during the exotherm). No transitions at lower temperatures were observed. A much broader, stronger exotherm began at 415°C, peaked at 550°C (66% weight loss at the peak), and the associated weight loss ended at 682°C (98% total weight loss). At a heating rate of 2°C/min without aluminum oxide in the sample crucible (68.5 mg sample weight), the sharp exotherm began at 208°C, peaked at 265°C, and the associated weight loss ended at 281°C (24% weight loss during the exotherm). No transitions at lower temperatures were observed. The broader, stronger exotherm began at 380°C, peaked at 504°C (63% weight loss at the peak), and the associated weight loss ended at 590°C (96% total weight loss).

Dry Nitrogen Tests. At a heating rate of 8°C/min with aluminum oxide present in the sample crucible (44 mg sample weight), a sharp, strong exotherm began at 225°C, peaked at 285°C (11% weight loss at the peak) and the transition ended at 330°C. No lower-temperature transitions were observed. A weight loss of 20% occurred during the exotherm, but the TGA curve declined gradually up to 510°C without a clear "plateau" in the plot and without any further deviation from the baseline of the DTA curve (21 mg (48%) of sample remaining). Only an additional 3 mg of sample was lost between 510°C and 850°C, while the DTA curve gradually drifted in an exothermic direction. There was no broad, strong exotherm recorded between 350° and 600°C as had been observed in the dry air runs. Substantial carbon was present in the sample crucible at the conclusion of the experiment (41% of the original sample weight remaining). At a heating rate of 2°C/min (86.9 mg sample weight) without aluminum oxide in the sample crucible, the sharp, strong exotherm began at 230°C and peaked at 278°C (6% weight loss at the peak). No lower-temperature transitions were observed. A weight loss of 8% occurred with a definite break (but not a plateau) in the TGA curve at the termination of the exotherm (281°C). The TGA continued a slow, downward drift until the termination of the experiment (410°C) without further deviation of the DTA from the baseline. At the 410°C termination temperature, 63% of the original sample weight remained and significant carbon was observed in the sample crucible.

Analyses of 1,3,5-Tricyanopentane

Dry Air Tests. The first run, performed under dry air at a heating rate of 8°C/min with aluminum oxide in the sample crucible (79.7 mg sample weight), exhibited a weak, broad exotherm peaking at 262°C with a weight loss of 6%. A sharp, strong endotherm immediately followed the exotherm and peaked at 371°C with a total weight loss of 78% at the peak. As the TGA curve indicated 99% of the original sample weight was lost by 389°C, the remainder of the curves after the sharp endotherm was neglected. Analysis of the model with aluminum oxide in the sample crucible and a heating rate of 4°C/min (60.6 mg sample weight) exhibited the broad, weak exotherm (peak at 260°C (8% weight loss)) and the following sharp, strong endotherm (peak at 340°C (57% weight loss to peak)). At 356°C, the TGA curve revealed that 58 mg (96%) of the model had been lost.

Dry Nitrogen Tests. At a heating rate of 8°C/min with aluminum oxide in the sample crucible (74.4 mg sample weight) and under dry nitrogen, the DTA/TGA of the model exhibited a weak, broad exotherm (250°C at peak, 4% weight loss)) and a sharp, strong endotherm (380°C at peak, 85% weight loss). The TGA curve leveled at 390°C, with only 2% of the original sample weight remaining. The DTA/TGA curves were very similar in appearance to those conducted with dry air. A repetition of the experiment (65.8 mg sample weight), but without aluminum oxide in the sample crucible, gave the

same exothermic (260°C at peak, 7% weight loss) and endothermic (380°C at peak, 99% weight loss) processes.

Analyses of 2,4,6-Tricyanoheptane

Dry Air Tests. With aluminum oxide in the sample crucible, a dry air atmosphere, and a heating rate of 8°C/min (65.3 mg sample weight), the DTA/TGA analysis of the model revealed a sharp, weak endotherm at a peak temperature of 40°C (no weight loss, melting point of the model), a weak, broad exotherm at a peak temperature of 262°C (18% weight loss), and a strong, sharp endotherm at a peak temperature of 330°C (77% weight loss). At 335°C, only 0.4% of the original sample remained, and thus the plots above 335°C were neglected. The curves were very similar in appearance to those obtained under similar conditions with the 1,3,5-tricyanopentane. The experiment when repeated at a heating rate of 4°C/min (31.9 mg sample weight) gave a similar exotherm (220°C, 12% weight loss) and endotherm (304°C, 97% weight loss). At 308°C, no sample remained.

Dry Nitrogen Tests. The first experiment was conducted at a heating rate of 8°C/min with a sample weight of 69.6 mg and using aluminum oxide in the sample crucible. Characteristics of the DTA/TGA were a sharp, weak endotherm peaking at 50°C (no weight loss, melting point of the model), a broad, weak exotherm peaking at 268°C (14% weight loss), and a sharp, strong endotherm peaking at 338°C (83% weight loss). At 355°C, the TGA curve leveled off with 99% of the

starting material consumed. Thus the DTA/TGA of 2,4,6-tricyanoheptane under nitrogen was nearly overlapping with that under air, and was also similar in appearance (but not in endothermic peak values and corresponding weight losses) to those of 1,3,5-tricyanopentane. Repetition of the experiment with aluminum oxide excluded from the sample crucible (71.6 mg sample weight) revealed a mp endotherm peaking at 55°C (no weight loss), a broad, weak exotherm peaking at 247°C (5% weight loss), and a second endotherm (sharp, strong) peaking at 355°C (92% weight loss). At 358°C, 98% of the original sample weight had been lost. In a third experiment, the sample (75.8 mg) was heated without aluminum oxide in the sample crucible at 10°C/min up to 175°C, and the instrument then adjusted to a heating rate of 1°C/min. The DTA/TGA exhibited a mp endotherm at 51°C (no weight loss), a broad, weak exotherm reaching a summit at 230°C (17% weight loss), a broad, strong endotherm peaking at 290°C (94% weight loss), and a 99% weight loss at 291°C.

Analyses of 2,4,6,8-Tetracyanononane

Dry Air Tests. The initial test conducted for the impure 4-unit model involved a heating rate of 4°C/min, a sample weight of 70.0 mg, and aluminum oxide in the sample crucible. A broad, strong exotherm began at 244°C and peaked at 340°C (33% weight loss to the peak). A sharp, strong endotherm that reached a summit at 372°C (50% weight loss to the peak) immediately followed the exotherm. The TGA

curve changed to a more gradual slope at 395°C (78% weight loss) and continued at about the same slope through a broad, strong exotherm beginning at 430°C, peaking at 471°C (84% total weight loss to the peak), and ending at 542°C (94% weight loss to the end of the exotherm). Complete loss of weight occurred by 591°C. A repeat of the experiment at 8°C/min (70.2 mg sample weight) gave a sharper initial exotherm that began at 255°C and peaked at 350°C (33% weight loss to the peak). A strong endotherm immediately followed the exotherm, peaking at 390°C with a 46% weight loss to the peak. The second major exotherm began at 445°C, peaked at 495°C (87% weight loss to the peak), and ended at 562°C (94% weight loss to the end of the exotherm). Complete loss of weight occurred by 638°C.

Dry Nitrogen Tests. The experiment was performed with a heating rate of 8°C/min, a sample weight of 62.8 mg, and with aluminum oxide in the sample crucible. An initial exotherm was broad and weak, beginning at 295°C, with a summit at 368°C (54% weight loss). A sharp, weak endotherm directly followed the exotherm and peaked at 391°C (81% weight loss). No second major exotherm in the 400-450°C region occurred, with the TGA curve essentially leveling out at 450°C (96% weight loss). The lack of a second exotherm at high temperatures (present with dry air) corresponded to the results obtained with polyacrylonitrile. Some carbon was observed in the sample crucible on termination of the run (800°C).

^{13}C-NMR Analyses of PAN Models

Procedure

All of the samples were dissolved in $CDCl_3$ at a concentration of 375-500 mg/ml. With the exception of 1 off-resonance spectra of 1,3,5-tricyanopentane, all of the ^{13}C-nmr's were proton-decoupled. The positions were reported in ppm relative to internal TMS standard (designated as 0.0 ppm). All of the spectra were obtained at room temperature except for 1 of 2,4,6-tricyanoheptane that was run at 50°C. Assignments for the model carbons were made by considering the positions of the carbon absorptions for the simpler analogues and from literature emperical rules and spectra[339-343].

1,3-Dicyanopropane (Glutaronitrile)

The spectra gave peaks with per cent heights at 118.672 (86%, $\underline{C}\equiv N$), 21.538 (43%, (X)$C\underline{C}H_2C$(X)), and 16.320 (77%, $CH_2\underline{C}H_2CN$) ppm. The spectrum was consistent with that reported in the literature[392].

1,3-Dicyanobutane

The complicated ^{13}C-nmr spectrum exhibited absorptions at 121.468 (67%, CH($\underline{C}N$)), 118.551 (73%, $CH_2\underline{C}N$), 29.365 (55%, (X)$C\underline{C}H_2C$(X)), 24.693 (76%, $\underline{C}H(CN)$), 17.352 (46%, $\underline{C}H_3$), and 15.107 (47%, $\underline{C}H_2CN$) ppm.

1,3,5-Tricyanopentane

Proton-decoupled. The spectrum obtained was relatively uncomplicated, revealing peaks at 119.279 (36%, CH$\underline{C}N$), 118.493 (81%, $CH_2\underline{C}N$), 29.910 (30%, $\underline{C}HCN$), 27.241 (39%, $\underline{C}H_2$), and 15.167 (40%, $\underline{C}H_2CN$) ppm.

Off-resonance. The spectrum was obtained with off-resonance spin-decoupling, i.e., with partial restoration of the ^{1}H - ^{13}C coupling and subsequent n + 1 splitting pattern (n equal to the number of protons attached to the carbon atom)[387]. Absorptions in the spectrum were at 119.279 (s, CH$\underline{C}$N), 118.493 (s, $CH_2\underline{C}N$), 29.910 (d, $\underline{C}H(CN)$), 27.241 (t, (X)C$\underline{C}H_2$C(X)), and 15.167 (t, $\underline{C}H_2CN$) ppm.

2,4,6-Tricyanoheptane

Since 3 stereoisomers were possible, a d,l-pair (atactic) and 2 meso-configurations (isotactic and syndiotactic)), the spectra was extremely complicated. Literature results show that sets of stereoisomers (but not enantiomers) give distinguishable peaks by ^{13}C-nmr[343]. For the 3-unit model, there were 3 peaks obtained for the nitrile carbons: 121.585 (33%, $CH_3CH(\underline{C}N)$, 1 stereoisomer), 121.284 (56%, $CH_3CH(\underline{C}N)$, a second stereoisomer), and 119.464 (49%, CH_2-$CH(\underline{C}N)CH_2$, both stereoisomers) ppm. The next absorption group (for the $CH_2\underline{C}H(CN)CH_2$ functionality) contained 4 peaks: 36.038 (34%, 2 overlapping peaks), 35.492 (22%), and 34.946 (19%). The third band included 3 distinct absorptions: 28.940 (15%, first (X)C$\underline{C}H_2$C(X) of atactic), 28.091 (20%, second (X)C$\underline{C}H_2$C(X) of atactic), and 26.998 (10%, (X)C$\underline{C}H_2$-C(X) of syndiotactic) ppm. The fourth group contained only 2 peaks: 24.147 (42%, $CH_3\underline{C}H(CN)$ of 1 stereoisomer) and 23.237 (33%, $CH_3\underline{C}H(CN)$ of second stereoisomer) ppm. The fifth and final band also contained 2 peaks, and was similar

in appearance to the fourth group: 18.019 (41%, $\underline{C}H_3CH(CN)$ of 1 stereoisomer) and 17.412 (29%, $\underline{C}H_3CH(CN)$ of a second stereoisomer) ppm. From the ^{13}C-spectra and from molecular model considerations of the sp^2 carbanion intermediates formed during the synthetic reaction sequence and the relative steric stabilities of the 3 possible isomers, it appeared that the d,l-pair (atactic) and 1 meso- stereoisomer (syndiotactic) had been preferentially formed.

The ^{13}C-nmr spectrum was rerun at 50°C to determine if any of the peaks obtained at room temperature were due to rotational isomers. The spectrum was overlapping peak-for-peak with the room temperature spectrum.

Syntheses of PAN Models, Related Chemistry

Decarbalkoxylation of Reactive Esters

Ethyl Phenylacetate, Method I. The procedure was similar to that of Krapcho and Lovey[346], except that no sodium chloride was used. A 250-ml, 3-neck round bottom flask containing a Teflon-coated stirring bar was equipped with a condenser topped by a vacuum adaptor, an internal thermometer, and a glass-ground stopper. Into the flask were placed 65 ml of dimethyl sulfoxide (Aldrich), 26.69 g (0.126 mole) of diethyl phenylmalonate (Aldrich), and 4.47 g (0.248 mole) of distilled water. An aqueous barium hydroxide solution was fitted to the vacuum adaptor and utilized as a gas trap (see the synthesis of 2,4,6-tricyanoheptane for description). Carbon monoxide began to evolve at a pot temperature of

146°C, the temperature reached a maximum of 155°C and then fell to 149°C, and ca. 10 hr was required to totally remove the carbon dioxide. The DMSO solution was poured into 400 ml of distilled water and the mixture extracted with 4-175 ml aliquots of ethyl ether. The ether extracts were combined over anhydrous magnesium sulfate for drying (19 hr), the salt filtered by aspirator suction, and the ether removed by rotary evaporation (aspirator pressure). Distillation yielded 3 fractions boiling from 65-71°C at 0.5 mm, and 1 fraction boiling at 74-75°C at 0.2 mm (lit.[393] bp of ethyl phenylacetate, 120-121°C (20 mm)). By nmr analysis, the lower-boiling fractions were contaminated with DMSO, and the higher-boiling ones with both DMSO and diethyl phenylmalonate. The nmr spectra (neat, internal TMS) differentiated the DMSO (92.18 ppm, sharp s, $(\underline{CH}_3)_2S{=}O$), diethyl phenylmalonate (7.20 ppm, band with spikes, aromatic $\underline{CH}$; 4.67 ppm, s, $C_6H_5\underline{CH}(X)_2$; 4.05 ppm, q, $O\underline{CH}_2CH_3$; and 1.00 ppm, t, $OCH_2\underline{CH}_3$), and ethyl phenylacetate (7.20 ppm, band with spikes, aromatic $\underline{CH}$; 4.05 ppm, q, $O\underline{CH}_2CH_3$; 3.50 ppm, sharp s, $C_6H_5\underline{CH}_2(X)$; and 1.00 ppm, t, $OCH_2\underline{CH}_3$) peaks. Nmr integration analysis showed the fractions to contain a total of 0.1 g (0.4% of starting material) of diethyl phenylmalonate, and 19.9 g (96%) of ethyl phenylacetate. Most of the latter was contained in the fractions boiling at 65-71°C (0.5 mm).

Ethyl Phenylacetate, Method II. The apparatus was the same as in Method I, except that the condenser was replaced

by a Claisen distilling head with built-in cold finger, Vigreux column, and vacuum take-off. Into the flask were placed 65 ml of dimethyl sulfoxide (Aldrich), 29.97 g (0.127) mole) of diethyl phenylmalonate (Aldrich), and 4.53 g (0.251 mole) of distilled water. The CO_2 gas trap, attached to the vacuum adaptor of the distilling head, showed carbon monoxide to be evolving at a solution temperature of 146°C. The stopcock of the distilling head was opened, the low-boiling, refluxing liquid mixture removed (bp 77-100°C) until the pot temperature rose to 175°C,and the stopcock then closed. After 2 hr at 175°C, no carbon dioxide could be detected with fresh barium hydroxide solution, and the system was cooled. Work-up of the reaction solution was the same as in Method I. Distillation gave 4 fractions boiling from 59-76°C, all at 0.4 mm (lit.[393] bp of ethyl phenylacetate, 120-121°C at 20 mm). Impurities were present as in Method I, with nmr integration analysis showing the fractions to contain a total of 0.3 g (1% of starting material) of diethyl phenylmalonate and 19.5 g (93%) of ethyl phenylacetate (see Method I for nmr peak positions). Most of the product was contained in the fractions boiling at 59-65°C (0.4 mm). Nmr analysis (neat, internal TMS) of the low-boiling distillate (4.61 g, bp 77-100°C) removed during reaction revealed that the material consisted of 2.7 g of water (broad s, 4.67 ppm, $\underline{H}OH$), 1.8 g of ethanol (broad s, 4.67 ppm, $O\underline{H}$; q, 3.70 ppm, $CH_3C\underline{H}_2O$; and t, 1.18 ppm, $C\underline{H}_3CH_2$), and 0.1 g of DMSO (s, 2.83 ppm, $(C\underline{H}_3)_2S{=}O$).

Ethyl Phenylacetate, Method III. The procedure was similar to that of Krapcho and coworkers[345], but without sodium cyanide. After drying over anhydrous barium oxide for 24 hr, 90 ml of commercial dimethyl sulfoxide (Aldrich) was filtered by aspirator suction and placed in a dry, 250-ml, 3-neck round bottom flask. The flask was equipped with a Claisen distilling head with built-in cold finger, Vigreux column, and vacuum take-off, a rubber septum, and a ground-glass stopper. A nitrogen oil bubbler was attached to the vacuum take-off of the distilling head, and ca. 5 g of calcium hydride (Fisher) and several mg of triphenylmethane (Aldrich) were added to the flask. Nitrogen was introduced into the system via a needle inserted through the rubber septum, and the solution refluxed for 17 hr under nitrogen until the dark red color of the triphenyl methyl anion was persistent. A second, dry 3-neck, 250-ml round bottom flask was equipped with 2 2-neck adaptors, the first adaptor containing a dropping funnel holding 10.73 g (0.045 mole) of diethyl phenylmalonate (Aldrich, dried over anhydrous magnesium sulfate for 12 hr) and a rubber septum, and the second adaptor containing an internal thermometer and a condenser topped by a glass-ground stopper. The nitrogen oil bubbler hose was removed from the Claisen head of the DMSO system, a vacuum line attached, and the dried DMSO distilled directly (89°C at 29 mm) into the second 3-neck flask via the remaining receiver neck. Approximately 50 ml of solvent was distilled into the flask. The

ground-glass stopper in the condenser was replaced with a vacuum adaptor attached to an aqueous barium hydroxide gas trap (see Method I), the nitrogen needle inserted into the rubber septum, and the gas flow started. The diethyl phenylmalonate was added, heating begun, and carbon dioxide evolution observed to commence at 178°C. The pot temperature rose to 190°C, held at that temperature for several hours, and then slowly decreased to 163°C. The evolution of carbon dioxide ceased after ca. 10 hr, the opaque, red solution was placed in 250 ml of distilled water, and the aqueous solution extracted with 4-175 ml aliquots of ethyl ether. The ether extracts were dried (anhydrous magnesium sulfate, 12 hr), filtered, and the solvent removed by rotary evaporation (aspirator pressure). Distillation gave 5 fractions collected between 28°C and 110°C, all at 0.4 mm (lit.[393] bp of ethyl phenylacetate, 120-121°C (20mm)). Nmr peak analysis showed DMSO and ethyl phenylacetate as being present (see Method I for nmr peak locations). Nmr integration analysis showed the fractions to contain 5.8 g (78%) of ethyl phenylacetate. Most of the product was contained in the fractions boiling at 57-70°C (0.4 mm).

Acetonitrile. The apparatus and general procedure were the same as in the synthesis of ethyl phenylacetate, Method I, except that a 500-ml, 3-neck round bottom reaction flask was used. Into the pot were placed 150 ml of dimethyl sulfoxide (Aldrich), 30.31 g (0.27 mole) of ethyl cyanoacetate

(Eastman) and 10.76 g (0.60 mole) of distilled water. Carbon dioxide began to evolve at a pot temperature of 150°C, the temperature rose briefly to 152°C, and decreased to 142°C over the reaction period. After 7 hr, no carbon dioxide could be detected, the flask was cooled, and the solution distilled directly at atmospheric pressure untilizing a Vigreux column. Five fractions were collected from 76°C to 175°C at 760 mm (lit.[394] bp of acetonitrile, 80.6°C). Nmr analysis (neat, internal TMS) revealed that H_2O (4.05 ppm, s, HOH), ethanol (4.05 ppm, s, OH; 3.65 ppm, q, OCH_2CH_3; 1.15 ppm, t, OCH_2CH_3), DMSO (2.68 ppm, s, $CH_3S{=}O$), and acetonitrile (2.00 ppm, s, CH_3CN) were present in varying amounts in the fractions, with the majority of the acetonitrile being distilled in the 76-97°C range. Nmr integration analysis showed that a total of 8.6 g (78%) of acetonitrile was isolated. No ethyl cyanoacetate was detected.

Cyclopentanone. The 2-carbalkoxy cyclopentanone used in the synthesis (Columbia Org. Chem.) was shown by nmr analysis (neat, internal TMS) to contain 63% of 2-carbethoxycyclopentanone and 37% of 2-carbmethoxycyclopentanone: 4.18 (q, OCH_2CH_3), 3.68 (sharp s, OCH_3), 3.20 (m, $CH_2CH(X)$-C=O), 2.20 (m, ring alkane CH_2) and 1.24 (t, OCH_2CH_3) ppm. The apparatus and general procedure were the same as for the synthesis of ethyl phenylacetate, Run I. Into the reaction flask were placed 29.84 g (0.12 mole of 2-carbethoxycyclopentanone and 0.078 mole of 2-carbmethoxycyclopentanone) of

2-carbalkoxycyclopentanone (Columbia Org. Chem.), 120 ml of dimethyl sulfoxide (Aldrich), and 10.88 g (0.60 mole) of distilled water. Carbon dioxide evolution became profuse at a pot temperature of 120°C, the temperature rose gradually to 142°C, and a total reaction time of 5 hr was required to remove all of the carbon dioxide. The reaction mixture was poured into 300 ml of distilled water, the aqueous solution extracted with ethyl ether, the combined extracts dried (anhydrous magnesium sulfate, 20 hr), and the salt filtered (gravity). The mixture was distilled using a Vigreux column at atmospheric pressure, giving (after removal of the ethyl ether, bp 35-37°C) 5 fractions boiling between 60°C and 190°C (lit.[395] bp of cyclopentanone, 131°C at 760 mm). Nmr analysis (neat, internal TMS) showed the presence of ethanol and DMSO (see synthesis of ethyl phenylmalonate for nmr chemical shifts), 2-carbethoxycyclopentanone and 2-carbmethoxycyclopentanone (see above for chemical shifts), and cyclopentanone (1.92 ppm, broad overlapping d, $C\underline{H}_2C{=}O$ and $C\underline{H}_2CH_2C{=}O$) in varying proportions in the fractions. Nmr integration analysis showed that 0.4 g (3.5% of starting material) of 2-carbmethoxycyclopentanone and 0.6 g (3% of starting material) of 2-carbethoxycyclopentanone were recovered, and that 12.5 g (75% based on starting material; 78% based on recovered starting material) of cyclopentanone were isolated.

Azine Syntheses

Benzalazine. Benzaldehyde semicarbazone was prepared

by a procedure similar to that of Shriner, Fuson, and Curtin[389]. Into a 3-neck, 2-liter round bottom flask fitted with a condenser and two ground-glass stoppers were placed 52.08 g (0.49 mole) of benzaldehyde (Eastman), 500 ml of absolute ethanol (Fsiher), and a Teflon-coated stirring bar. Distilled water was added until the solution became faintly turbid, and the turbidity just removed by dropwise addition of ethanol. Additions of 50.00 g (0.45 mole) of semicarbazide-hydrochloride (Eastman, mp 173°C) and 75.00 g (0.55 mole) of sodium acetate (Baker) were made, and the resulting solution heated on a steam bath for 2 hr with vigorous stirring. During the heating, needle crystals of product began to precipitate from the hot solution. An additional aliquot of 500 ml of distilled water was then added, the mixture heated for 30 min, and the system cooled (ice bath) to precipitate the remainder of the crystalline product. The solid was recrystallized from a 25% ethanol-water solution to give 60.2 g (83%) of white, crystalline benzaldehyde semicarbazone: mp 214-215°C (lit.[392] mp 222°C).

Into a 3-neck, 100 ml round bottom flask containing a Teflon-coated stirring bar and fitted with a condenser topped by a vacuum adaptor, an internal thermometer, and a ground-glass stopper were placed 5.00 g (0.031 mole) of benzaldehyde semicarbazone, 20 ml of dimethyl sulfoxide (Aldrich), and 1.30 g (0.072 mole) of distilled water. A saturated aqueous barium hydroxide solution was attached to the vacuum adaptor as a gas trap (see the synthesis of 2,4,6-tricyanoheptane

for description), and the flask heated rapidly with vigorous stirring. Carbon dioxide began to evolve at 150°C, the pot temperature leveled at 160-162°C, and the system was held at that temperature. The gas trap was removed before clogging, and reattached with fresh solution periodically until no more gas evolution was observed (2½ hr). An unidentified, vile-smelling white solid was observed to have formed on the condenser wall. Copious distilled water was added to the DMSO solution to precipitate the azine as a fine yellow powder, the solid filtered by aspirator suction, and the powder recrystallized to uniform yellow needle crystals from methanol (Fisher, 2 repetitions). A total of 1.42 g (44%) of recrystallized benzalazine was obtained: mp 92.7-93°C (lit.[362] mp 92°C); nmr peaks ($CDCl_3$, external TMS) at 9.00 (2H, sharp s, $C_6H_5C\underline{H}=N$), 8.11 (4H, m, aromatic $C\underline{H}=C-CH=N$), and 7.72 (6H, m, aromatic $C\underline{H}$) ppm; ir absorptions (KBr pellet) at 3030 (aromatic C-H), 2930 (C-H), 1675 and 1650 (C=N), 1550, 1480 (aromatic C-H), 1293 and 1210 (azine), 960 (aromatic C=C), 850 (C=N), 750 (azine), and 685 (aromatic C=C) cm^{-1} (overlapping with lit.[393] ir spectra); and mass spectral peaks with relative abundances at m/e 208 (parent ion, 61%), 180 (34%), 131 (100%), 104 (45%), 77 (67%), and 51 (35%) (overlapping with lit.[394] mass spectra).

Elemental analysis for $C_{14}H_{12}N_2$:

Calculated:	C, 80.74; H, 5.81
Found:	C, 79.61; H, 5.64

Benzophenonazine, Method I. The apparatus was the same as in the synthesis of benzalazine except that a N_2 oil bubbler was substituted for the barium hydroxide gas trap. Into the reaction flask were placed 20 ml of dimethyl sulfoxide (Eastman) and 5.21 g (0.027 mole) of benzophenone hydrazone (Fisher, mp 99-100°C). The system was brought to reflux and held for 19 hr. Moderate bubbling was observed during the heating period. After cooling, needle crystals precipitated from the dark red solution. The material was placed in 200 ml of distilled water, the aqueous layer extracted with 4-150 ml aliquots of methylene chloride, and the organic extracts placed over anhydrous magnesium sulfate for drying 11 hr). The salt was filtered by aspirator suction and the methylene chloride removed by rotary evaporation. The crude remains consisted of a yellow solid with dark red impurities. Recrystallization from ethyl acetate was performed to give uniform, yellow-tint crystalline rods. Washing with acetone removed most of the color to give 2.42 g (51%) of pale yellow, crystalline rods of benzophenonazine: mp 162-163°C (lit.[380] mp 162-163°C); nmr peaks ($CDCl_3$, external TMS) at 7.50 (s, with spikes, aromatic CH) ppm; ir absorptions (KBr pellet) at 3030 (aromatic C-H), 1525 (C=N), 1475 (aromatic CH), 1435 (-C=N), 950 (aromatic C=C), 760 (azine), and 680 (aromatic C=C) cm^{-1}; mass spectral peaks with relative abundances at m/e 360 (42%), 283 (82%), 205 (9%), 180 (90%), 165 (100%), 77 (88%), and 51 (37%) (overlapping with lit.[394] mass spectra).

Elemental analysis of $C_{26}H_{20}N_2$:

Calculated:	C, 86.63; H, 5.59
Found:	C, 86.11; H, 5.58
Lit.[380]:	C, 86.52; 5.59

Benzophenonazine, Method II. The procedure was the same as in Method I, except that the system was stirred at room temperature instead of reflux. Reactants were 5.10 g (0.026 mole) of benzophenone hydrazone (Fisher) and 20 ml of dimethyl sulfoxide (Eastman). After 3 weeks of stirring at room temperature, yellow solid began to separate. After cooling (-10°C) and when no further solid appeared to be separating, the material was filtered by aspirator suction and recrystallized from ethyl acetate to give orange tint, crystalline rods. After washing the solid with acetone, 3.35 g (72%) of pale yellow, crystalline rods of benzophenonazine were obtained. Analysis was the same as for the product isolated in Method I.

CHAPTER III

RESULTS AND DISCUSSION, POLYACRYLONITRILE MODELS

Syntheses of PAN Models

The main historical hindrance in the investigation of PAN models has been the lack of development of simple mild syntheses of the compounds. In particular, the conversion of the ester precursors of the models to the alkyl nitriles has resulted in low yields of impure products[317, 320, 329]. The novel methods detailed herein resulted in production of the pure (^{1}H- and ^{13}C-nmr, ir, mass spectra, and elemental analyses) 3-unit models (1,3,5-tricyanopentane (18) and 2,4,6-tricyanoheptane (19)), and in a new synthesis of the crude 4-unit model of PAN (2,4,6,8-tetracyanononane (20)). The presented procedures are expected to further facilitate studies of PAN models and comparison of their properties to those of the polymer[25, 336-338].

The flow diagram for the improved syntheses are shown in Figures 1 and 2, while the older procedures are outlined for comparison in Figures 3 and 4. In the latter, yields of the previous workers are contained in parentheses. Yields from new procedures detailed herein (Figures 1 and 2) are bracketed and starred in Figures 3 and 4, while yields from procedures performed by the author that were similar to those of the earlier workers are simply bracketed.

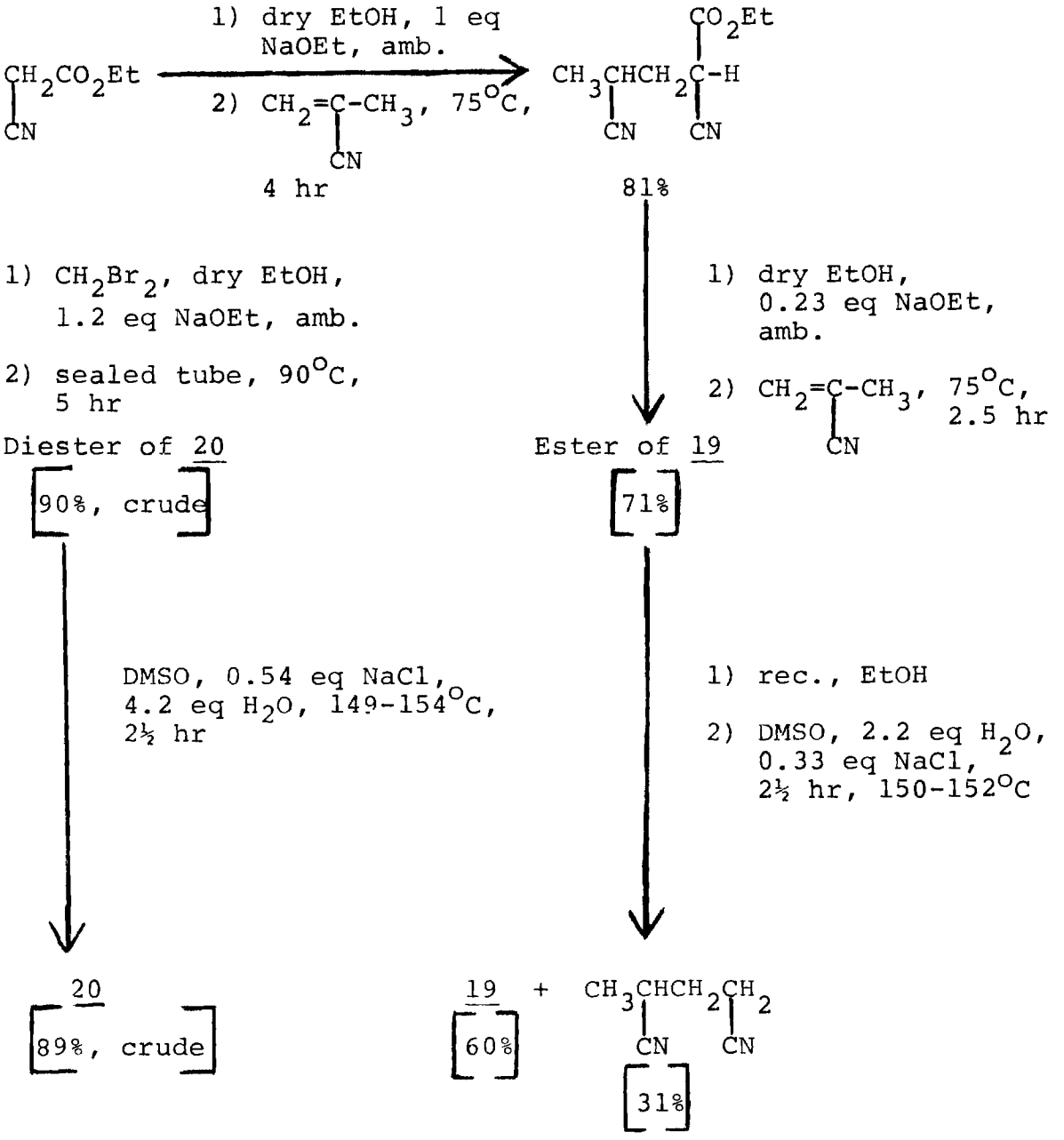


Figure 1. Flow Diagram of the Developed Syntheses of 2,4,6-Tricyanoheptane (19) and 2,4,6,8-Tetracyanononane (20).

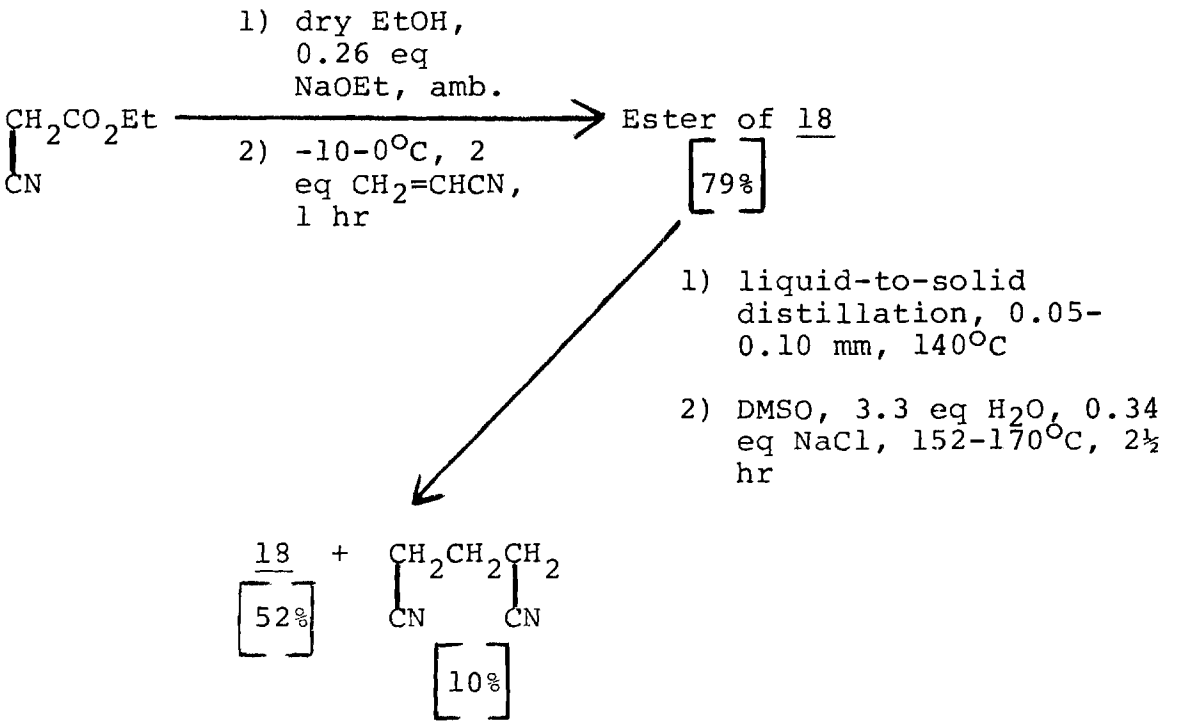


Figure 2. Flow Diagram of the Developed Synthesis of 1,3,5-Tricyanopentane (18).

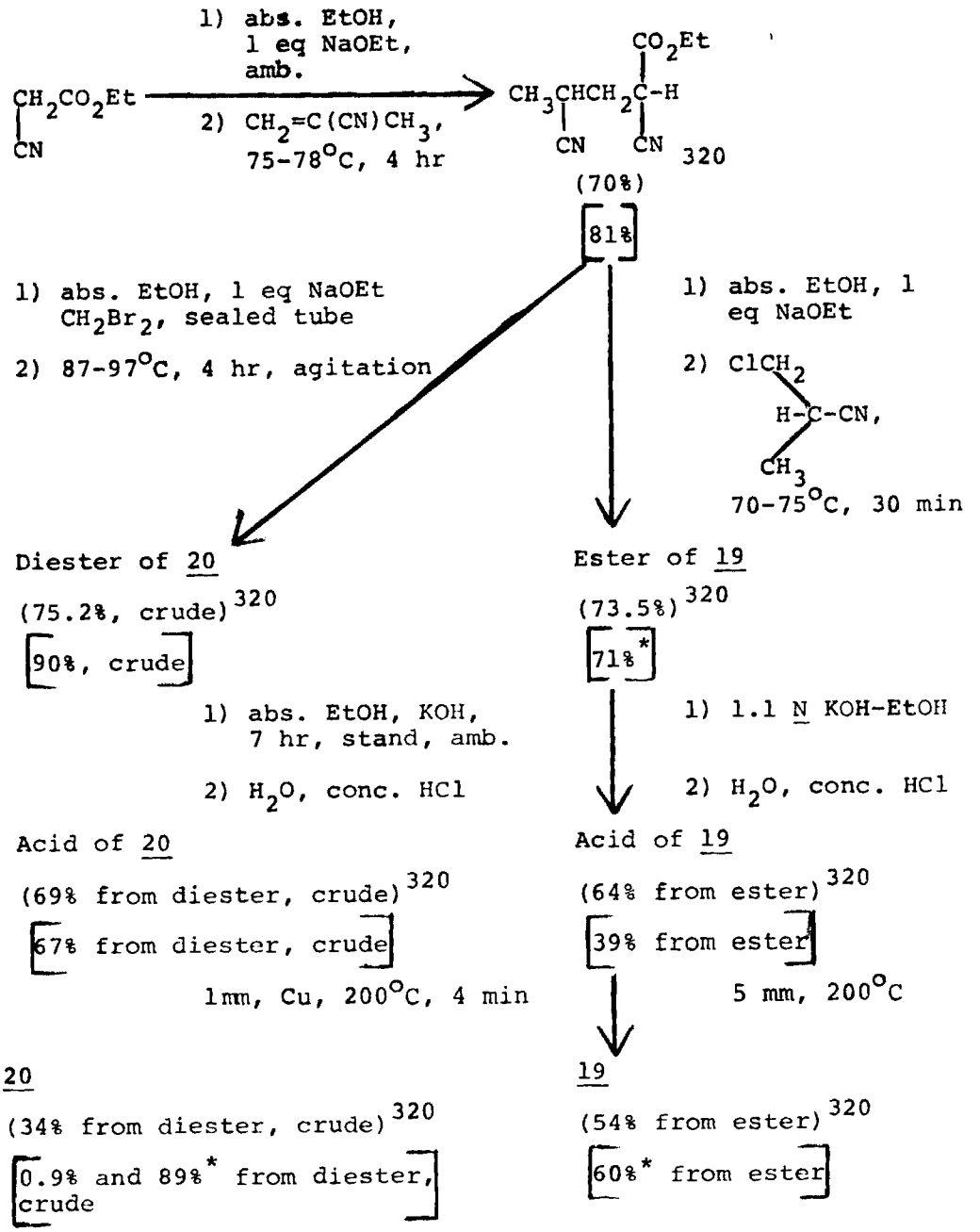


Figure 3. Flow Diagram of the Takata-Taniyama Syntheses of 2,4,6-Tricyanoheptane (19) and 2,4,6,8-Tetracyanononane (20).

*Denotes yields from the procedures developed herein.

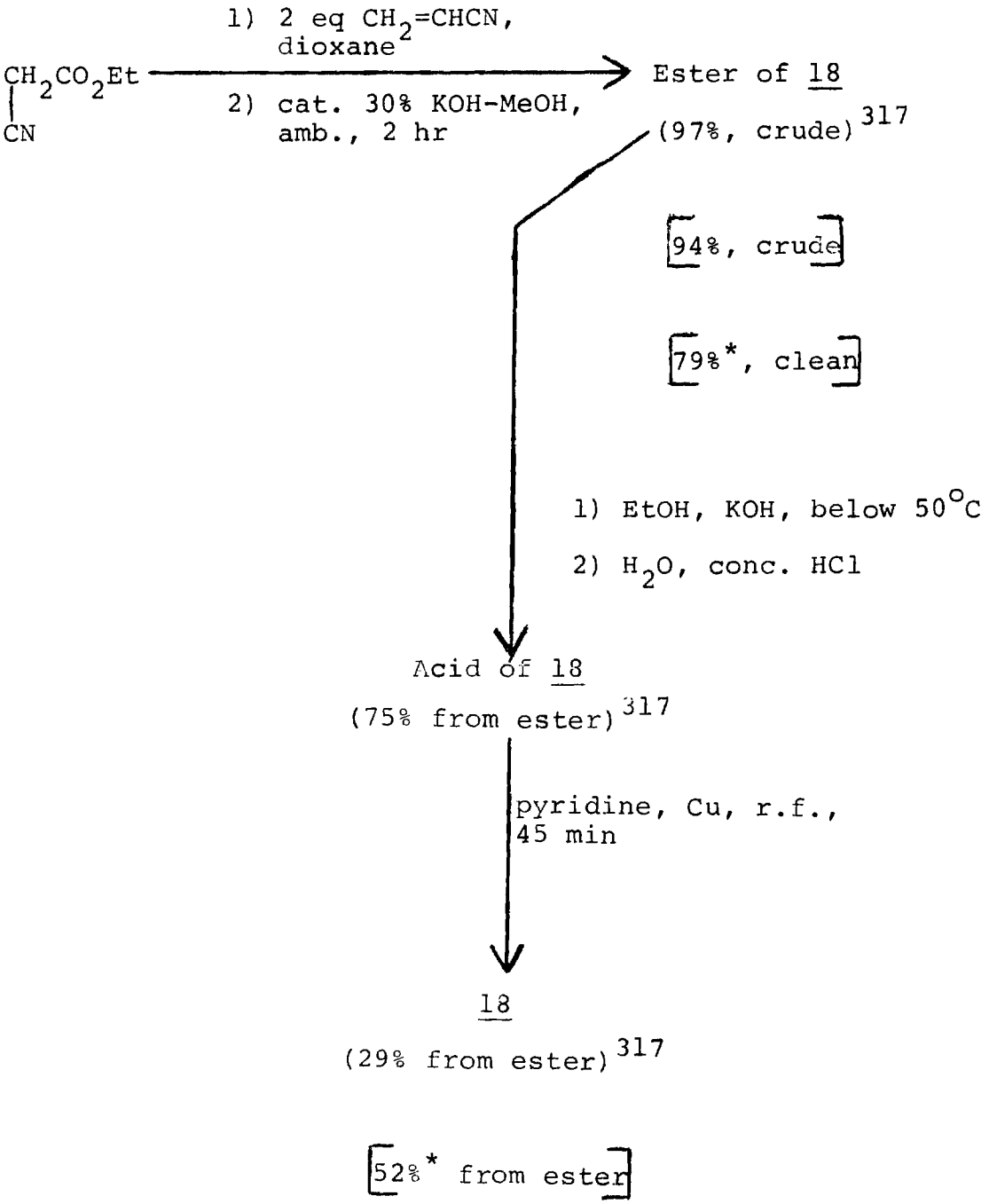
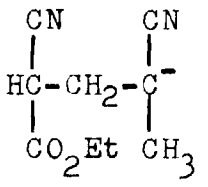


Figure 4. Flow Diagram of the Zahn-Schafer Synthesis of 1,3,5-Tricyanopentane (18).

*Denotes yields from the procedures developed herein.

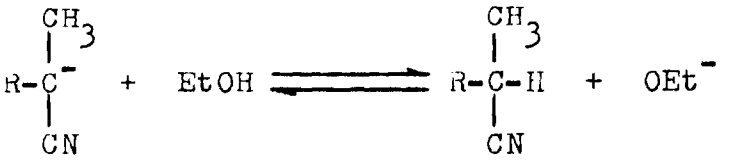
Synthesis of 2,4,6-Tricyanoheptane

Ethyl-2,4-Dicyanopentanoate. The synthesis as reported by Takata and Taniyama[320] resulted in a high yield of the product and was thus retained with little modification in the new procedures (Figures 1 and 3). The yield was improved slightly from that reported in the literature (81% vs. 70%[320]), and may have been due to the use of "super-dry"[388] instead of absolute ethanol, i.e., less residual water was present in the revised procedure to react with the sodium ethoxide. According to the rules set forth by House for Michael additions, catalytic amounts of as weak a base as possible, low temperatures, and short reaction times diminish side reactions, including reverse Michael addition[357]. However, lower temperatures for the ethyl-2,4-dicyanopentanoate synthesis led to recovery of starting material. The exotherm occurring around 75°C was thus indicative of the energy barrier hindering formation of the methylated (and hence somewhat destabilized[399]) carbanion, 28, from addition of the ethyl cyanoacetate carbanion to methacrylonitrile:



28

The difficulty in forming the product was contrasted by the facile addition of ethyl cyanoacetate carbanion to acrylonitrile at room temperature (see the synthesis of 3-carbethoxy-1,3,5-tricyanopentane for discussion). As detailed in the Experimental Section, as the base: ethyl cyanoacetate ratio was reduced below 1, the yield of the diadduct, 4-carbethoxy-2,4,6-tricyanoheptane, increased. Thus it was shown that a high reaction temperature, 1 mole equivalent of base, and comparatively long reaction times were necessary to attain a high yield of ethyl-2,4-dicyanopentanoate in the Takata-Taniyama procedure. The reason for the variation from the accepted Michael addition rules[357] lay in the complex set of equilibria existing in the mechanisms of formation of the mono- and diadducts. As each carbanion was formed and protonated, base was regenerated:



The ethyl-2,4-dicyanopentanoate contained an acidic hydrogen that could be removed to reform the carbanion, and thus generate the diadduct by further methacrylonitrile addition. With 1 equivalent of NaOEt present at the beginning of the reaction, a huge excess of base was in the system throughout the process.

Apparently, the excess base shifted the equilibria to the monoadduct, and thus use of 1 equivalent of NaOEt favored the formation of ethyl-2,4-dicyanopentanoate over 4-carbethoxy-2,4,6-tricyanoheptane.

4-Carbethoxy-2,4,6-Tricyanoheptane. Takata and Taniyama employed ethyl-2,4-dicyanopentanoate with NaOEt and 1-chloro-2-cyanopropane to produce the ester precursor of 19, supposedly by carbanion displacement of the halogen[320]. It was suspected, however, that the labile tertiary hydrogen in 1-chloro-2-cyanopropane, in conjunction with the strong ethoxide base, would facilitate ElcB elimination[400] to form methacrylonitrile in situ. The methacrylonitrile would then be attacked by the carbanion of ethyl-2,4-dicyanopentanoate in a Michael addition to give the desired product. It had been demonstrated in the modified synthesis of ethyl-2,4-dicyanopentanoate that catalytic amounts of base favored formation of the diadduct in a second Michael addition (see discussion in the preceding section). Synthesis of the diadduct directly from ethyl cyanoacetate and methacrylonitrile gave only a 17% yield of 4-carbethoxy-2,4,6-tricyanoheptane. However, when ethyl-2,4-dicyanopentanoate was utilized with NaOEt and methacrylonitrile (75°C, 4 hr), an 81% yield of 4-carbethoxy-2,4,6-tricyanoheptane was isolated (Figure 1). The yield was improved over that reported by the Japanese workers for the alternate route (81% vs. 70%), possibly due to the effect of the base concentration on the reaction equilibria (see the

discussion in the preceding section). Elimination of HCl or direct displacement of the chloride ion with the 1-chloro-2-cyanopropane (to form insoluble NaBr) would have altered the base concentration, and hence also the character of the equilibria. The low yield of diadduct in the direct synthesis from ethyl cyanoacetate may have resulted from the short reaction time in comparison to that of the adopted method (2 hr vs. 4 hr). No attempt was made to optimize the yield for the direct method.

2,4,6-Tricyanoheptane, 19. The yield obtained by Takata and Taniyama for the conversion of 4-carbethoxy-2,4,6-tricyanoheptane to the corresponding acid (64% reported) could not be duplicated (39% isolated in the present study). The older model synthesis was also undesirable due to the utilization of strong base and acid (both of which can hydrolyze nitriles in the presence of water under harsh conditions[344]), and to the high temperatures involved in the decarboxylation of the acid of 19 (Figure 3).[320]

Preliminary experiments with a simpler ester model (ethyl-2,4-dicyanopentanoate) demonstrated that high yields of pure 1,3-dicyanobutane (87%) could be obtained in 1 step by the adapted decarbalkoxylation procedure of Krapcho and Lovey[346]. Thus after recrystallizing the ester precursor of 19 from ethanol[320], the Krapcho-Lovey decarbalkoxylation procedure was utilized in the model synthesis (Figure 1)[346]. The 4-carbethoxy-2,4,6-tricyanoheptane was converted smoothly

to 19 in a single step. The yield was slightly higher than that obtained by the multi-step, strenuous Takata-Taniyama synthesis (60% vs. 54%[320]), and the only impurities detected by modern analytical techniques were weak ir bands in the 3575 and 1625 cm^{-1} regions. The same peaks were more pronounced in the ir spectra of the Japanese workers, and a weak carbonyl peak at ca. 1725 cm^{-1} was also apparent[320]. As the hygroscopic character of the multi-polar model was undetermined, the effect of adsorbed water (which exhibits bands at 3710 and 1630 cm^{-1})[401] on the ir spectra was unknown.

Substantial reverse Michael addition product, 2,4-dicyanobutane (31%, Figure 1) was formed in the decarbalkoxylation. The chloride ion was suspected of functioning as a strong base[356] in the DMSO under the reaction conditions to catalyze the reverse Michael addition as shown in Figure 5. Later studies (partially contained herein) showed that with reactive esters, e.g., ethyl cyanoacetate, NaCl was an unnecessary reagent in the Krapcho-Lovey method for decarbalkoxylation to occur[354-355]. A comparative study with 3-carbethoxy-1,3,5-tricyanopentane, however, showed that in the adapted Krapcho-Lovey procedure, a higher yield of 1,3-dicyanopropane, longer reaction times, and contamination of the isolated model with unreacted ester resulted when NaCl was omitted from the reaction flask (see the synthesis of 1,3,5-tricyanopentane for a more complete discussion). DMSO may have become sufficiently reactive under the conditions

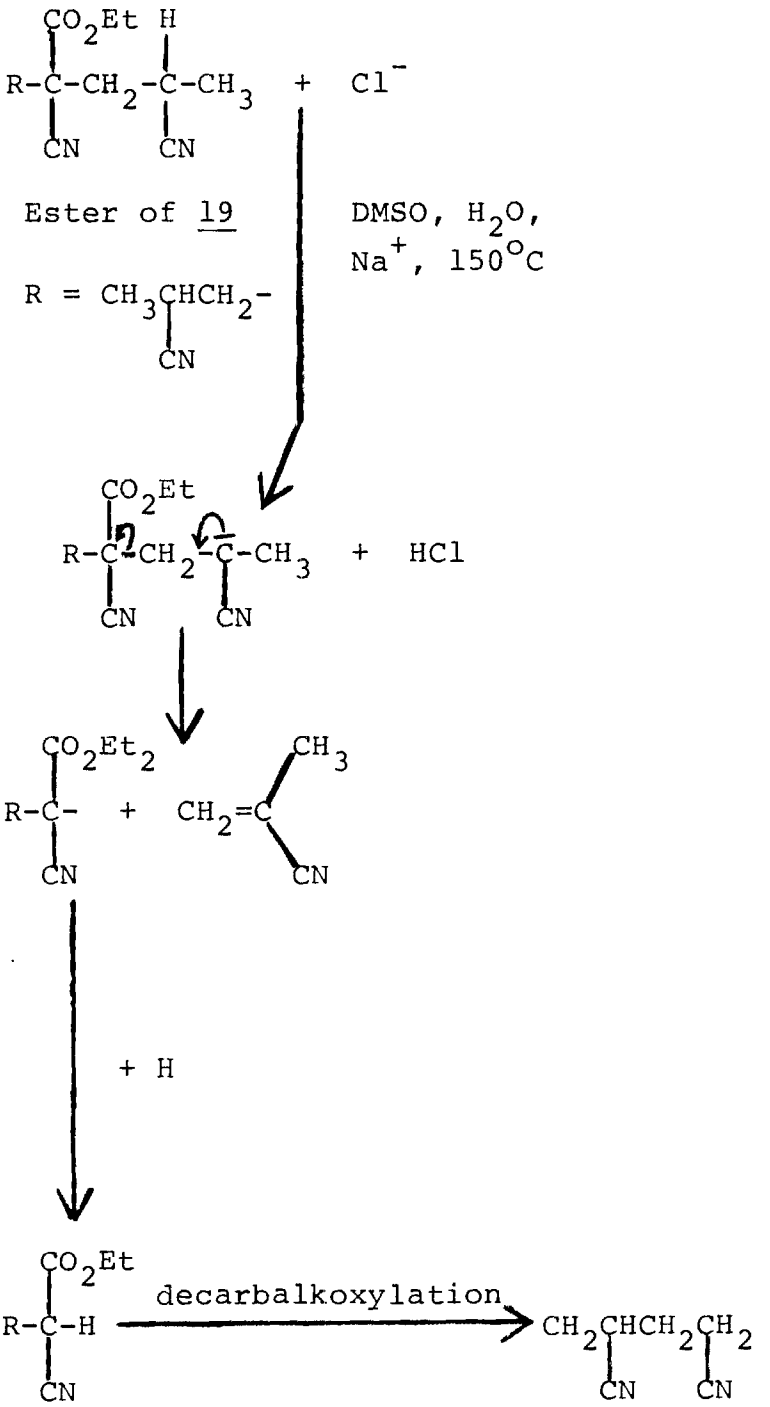
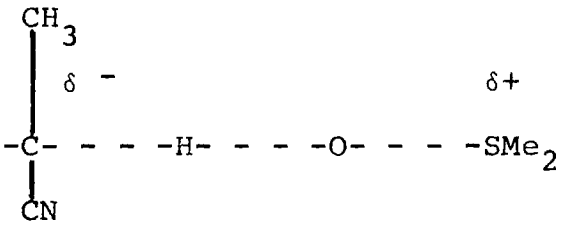


Figure 5. Possible Chloride-Catalyzed Reverse Michael Addition of PAN Models.

employed to abstract the hydrogen from the methine carbon and regenerate the carbanion, as in the decarboxylation mechanism postulated by Chen and Yan for tetrahalophthalic acid, 24[353]:



Synthesis of 2,4,6,8-Tetracyanononane, 20

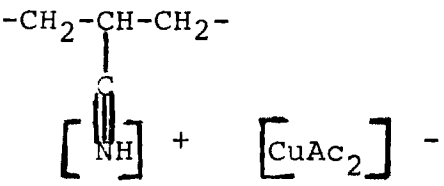
4,6-Dicarbethoxy-2,4,6,8-Tetracyanononane. After the synthesis of ehtyl-2,4-dicyanopentanoate was completed, attention was turned to preparation of the diester derivative of 2,4,6,8-tetracyanononane. The Takata-Taniyama synthesis[320] was repeated with an increase in yield of crude product (Figures 1 and 3). The agitation reported by the previous workers was found to be unnecessary. As reported[320], the high MW (372.47 g), multi-polar compound was undistillable, fragmenting and tarring before a bp was reached with high vacuum. Thin-layer chromatography (TLC) of all the PAN model ester precursors showed that the polar impurities and the product migrated as a single spot on the coated plate, thereby eliminating column chromatography as a purification method. Thus no method of purification could be developed for the dark red, uncrystallizable material, and the crude diester had to be employed in the remaining steps of the synthesis.

4,6-Dicarboxy-2,4,6,8-Tetracyanononane. The formation

of the potassium salt of the diester proceeded readily and in good yield (77%) by the Takata-Taniyama route[320]. Care was taken to keep the reaction flask cold to minimize nitrile hydrolysis. The diacid was obtained by hydrolysis of the potassium salt, again taking precautions to minimize amide or acid functionality formation. It appeared that substantial purification had resulted from the conversions, as the diacid crystallized to a white, wax-like solid. The ir and nmr spectra showed the $-CO_2H$ functionality to be present, and no absorptions due to underesterified material was observed. As for the diester, no further purification of the diacid was attempted (see the discussion in the previous section).

2,4,6,8-Tetracyanononane, 20. The production of the 4-unit model from the diacid was also initially after Takata and Taniyama[320]. The yield was exceptionally low (13% vs. 50%[320] from the diacid), with a black, tar-like, intractable substance being the main product of the decarbalkoxylation. Analytical techniques revealed impurities of the -N-H and/or -O-H, C=O, C=N, and C-O types. The elemental analysis indicated an extremely low carbon content (2.89% below the theoretical for the wax-like solid), a considerable deviation from that obtained by Takata and Taniyama (0.49% below the calculated value for 20)[320]. Incorporation of oxygen (atomic weight 16) would decrease the percentage of carbon in such a manner, and also result in higher MW substances. Indeed, mass spectra revealed substantial, unidentified

impurities of MW 212 and 195. The ir spectra of the previous authors showed impurity peaks that were considerably more prominent for the 4-unit model than the corresponding bands in the spectra reported for the 3-unit model[320]. The ir spectra of 20 synthesized in the present investigation corresponded to that of the previous workers. Thus it was evident that amides (and/or acid) and imine functionalities were present in the isolated model, the former arising due to acid and/or base hydrolysis of an unknown number of nitriles during the conversion of the diester to the diacid, and the latter by thermal cyclization of the nitriles during the decarbalkoxylation. Perkins, Gaulin, and coworkers have demonstrated that amide and acid groups are formed in the polymer on pyrolysis *via* attack of trapped oxygen in the solid substrate[176-182]. As the current system was thoroughly evacuated before and during decarbalkoxylation, it is unlikely that the minor O_2 present could have produced the substantial amide and acid impurities observed in the spectra. Grassie and McGuchan have demonstrated that isothermal heating of PAN at 200°C results in the nitrile-cyclized structure[281], and thus the tarring observed during the decarboxylation was expected. In addition, Moutald and Cauville have shown that PAN fibers fixated with Cu^+ ions result in shorter and more efficient processing in carbon fiber production, presumably due to cyclization initiation by the protonated nitrile, 29[288]:



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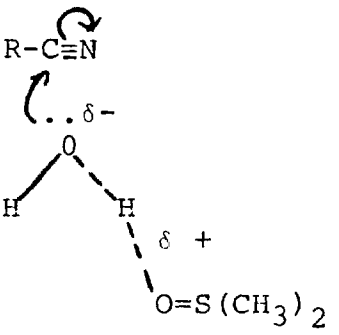
Facilitation of the nitrile polymerization by the copper metal used in the decarbalkoxylation was undetermined.

It was evident that pure 20 could not be obtained by the Takata-Taniyama procedure. Purification presented an insurmountable problem due to the high MW and polarity of the compound, and also the numerous theoretical combinations of partially-hydrolyzed alkyl nitriles that were conceivably present in the impure mixture. Adaptation of the Krapcho-Lovey decarbalkoxylation procedure[346] was thus attempted. The crude diester was employed, and an 89% yield of crude 20 (vs. 13% by the Takata-Taniyama method) was obtained. Nmr spectra showed that the absorptions due to the ester functionalities had disappeared, and that the integration ratio for the methine hydrogens had doubled, both indicating that decarbalkoxylation of the diester had proceeded successfully. Ir, however, revealed that the impurities present in the samples prepared by the older method were also present in the decarbalkoxylated material. Imine formation may have been due to nucleophilic attack of the nitriles by DMSO or its degradation products[358], as pure DMF[33-35] and dimethylsulfone[40] had been shown to initiate nitrile cyclization in PAN

at higher temperatures over long periods. The strong carbonyl absorptions were probably due to unreacted ester functionalities too dilute to be detected by nmr. The formation of -N-H (other than terminal imine groups) and/or -O-H and C=O functionalities possibly resulted from hydrolysis of some nitriles by the DMSO-H_2O system under the reaction conditions <u>via</u> the initiating species <u>30</u>:



<u>30</u>

However, absence of a carbonyl absorption in <u>19</u> or 1,3-dicyanobutane produced in similar fashion indicated insignificant nitrile hydrolysis in those systems, and the ir absorption in the imine range (1625 cm^{-1}) for <u>19</u> was weak. The increased degradation of <u>20</u> thus appeared to be due to the impurities carried over from the crude diester. The impurities probably acted as initiators for the nitrile cyclization[284-287] or presented unreactive ester or non-ester functionalities (or functionalities alterable under the reaction conditions to a group other than that desired), either of which would lower the purity of the isolated product. Some color purification was

accomplished on a small scale by the liquid-to-solid distillation technique developed in the synthesis of 3-carbethoxy-1,3,5-tricyanopentane (139°C, 0.1 mm). Nmr and ir spectra, however, showed no reduction in the impurity peaks. The impurities were thus co-collecting with the product, reemphasizing the TLC characteristics of the inseparable, multi-polar compounds produced in the model synthesis.

Synthesis of 1,3,5-Tricyanopentane, 18

3-Carbethoxy-1,3,5-Tricyanopentane. The crystalline ester precursor of 18 as produced by the Zahn-Schafer procedure[317] was a dark, brownish-black material. The ester appeared much less thermally stable than 4-carbethoxy-2,4,6-tricyanoheptane, tarring excessively before the bp was reached. The reported recrystallization from EtOH[312,317] was unsuccessful, as the low-melting ester oiled out of solution instead of solidifying. A variety of other common solvents were also unsuccessfully tested as recrystallization media. A liquid-to-solid distillation technique was thus developed that resulted in pure, white 3-carbethoxy-1,3,5-tricyanopentane (see the Experimental Section for a complete description of the procedure). The purification method, though yielding ester of excellent quality, was time-consuming, and thus its desirability was lessened.

Interest developed in the inability of earlier workers to isolate the monoalkylated product in the base-catalyzed Michael addition of ethyl cyanoacetate to acrylonitrile, even

in the presence of excess ester[311-312]. Attempted preparation of ethyl-2,4-dicyanobutanoate, utilizing the rules for Michael additions set forth by House[357], was unsuccessful. However, it was observed that "clean" diadduct (slight yellow tint, pure by analytical techniques) was obtained by the procedure (catalytic NaOEt-EtOH, short reaction times, cold temperatures (Figure 2)). The ester was distillable by conventional methods from the mixture with unreacted ethyl cyanoacetate without excessive tarring. The method was thus adapted successfully to the planned synthesis of the ester precursor of 18, with a slightly lowered yield from the Zahn-Schafer procedure (79% vs. 94%[317]), but with much greater purity of initial product. The material so produced was successfully decarbalkoxylated without further purification in the synthesis of 18. It was demonstrated, however, that the slight yellow color was removable by the liquid-to-solid distillation technique.

1,3,5-Tricyanopentane, 18. The model was produced readily from the ester by the adapted Krapcho-Lovey decarbalkoxylation method as with the synthesis of 19. The yellow-tinted crystals from the improved synthesis of the ester precursor were successfully utilized without further treatment. Minor impurities of the -N-H and -C=N types registered bands in the ir spectrum of the model, but were undetectable by other analytical techniques. The compound could not be crystallized, existing as a viscous oil[317]. The model 18 distilled at a

higher temperature than had 19, although the former was of lower MW (185-187°C (0.08 mm) and 156-160°C (0.1 mm), respectively). Apparently, the inductive effect of the end methyls had sufficiently reduced the polarity of the outer nitriles in 19 to lower its bp below that of the unmethylated 18. A greater tendency to tar near the bp was also exhibited by 18.

The yield of 18 by the presented method was much improved over that of the literature procedure (52% vs. 34%, Figure 4). The isolated yield was reduced not only by tarring near the bp, but also by formation of reverse Michael addition product, 1,3-dicyanopropane (10% yield), presumably by chloride ion or DMSO initiation under the reaction conditions (Figure 5). To determine whether the model ester precursors were sufficiently reactive to decarbalkoxylate without NaCl[354-355], and whether the chloride ion was totally responsible for the reverse Michael addition[356-357], an identical run to produce 18, but without added NaCl, was made. A longer heating period was required for significant CO_2 evolution to cease without the salt than in its presence (4.7 hr and 2.5 hr, respectively). Work-up gave a higher yield (30%) of 1,3-dicyanopropane than had been obtained with NaCl (10%). In addition, unreacted ester codistilled with the model as an impurity when salt was omitted, and the yield of model was reduced by 20%. The chloride ion, therefore, appeared to increase the rate of reaction for decarbalkoxylation of 3-carbethoxy-1,3,5-tricyanopentane, which indicated that the compound was less reactive

than other esters tested[354-355]. In other words, the dialkyl-substituted 3-carbon bearing the ester group of the model precursor was less susceptible to carbanion formation than the unsubstituted analog, ethyl cyanoacetate, which decarbalkoxylates readily to acetonitrile with the NaCl-deficient Krapcho-Lovey procedure (see the discussion for decarbalkoxylation of reactive esters and the synthesis of acetonitrile)[354]. Formation of 1,3-dicyanopropane in the absence of chloride ion confirmed that the DMSO system alone could initiate the carbanion formation necessary for reverse Michael addition. The longer reaction time, however, may have accounted for the increased yield of lower MW product, and thus the possibility of initiation of the reversal by both chloride ion and DMSO in competing processes was not discounted by the comparative experiment.

DTA/TGA Analyses of PAN and its Models

Several important observations were extracted from the DTA/TGA grapsh of pure 1,3,5-tricyanopentane (18), pure 2,4,6-tricyanoheptane (19), impure 2,4,6,8-tetracyanononane (20), and redox-initiated PAN (Tables 1 and 2). Pure 18 and 19 were produced by the developed syntheses, and the impure 20 utilized in the tests was made by the Takata-Taniyama method[320].

DTA/TGA of 1,3,5-Tricyanopentane (18) and 2,4,6-Tricyanoheptane (19).

The visual DTA/TGA characteristics of 18 and 19

Table 1. DTA/TGA Characteristics of Pure 1,3,5-Tricyanopentane (18) and Pure 2,4,6-Tricyanoheptane (19) in Dry Air and Dry Nitrogen.

Model	Wt. (mg)	Conditions: Stand. Sample Crucible	Conditions: Rate (°C/min)	Conditions: Atm. (dry)	Exotherm: Peak Temp. (°C)	Exotherm: Wt. Loss to Peak (% orig.)	Endotherm: Peak Temp. (°C)	Endotherm: Wt. Loss to Peak (% orig.)	Temp. (°C)	Wt. Loss (% orig.)
18	79.7	Al_2O_3	8	Air	262	6	371	78	389	99
18	60.6	Al_2O_3	4	Air	260	8	340	57	356	96
19	65.3	Al_2O_3	8	Air	262	18	330	77	335	100
19	31.9	Al_2O_3	4	Air	220	12	304	97	308	100
18	74.4	Al_2O_3	8	N_2	250	4	380	85	390	98
18	65.8	None	8	N_2	260	7	380	99	380	99
19	69.6	Al_2O_3	8	N_2	268	14	338	83	355	99
19	71.6	None	8	N_2	247	5	355	92	358	98
19	75.8	None	10,*	N_2	230	17	290	94	291	99

*Sample heated at 10°C/min up to 175°C, and then at 1°C/min for the remainder of the test.

Table 2. DTA/TGA Characteristics of Polyacrylonitrile and Impure 2,4,6,8-Tetracyanononane, 20, in Dry Air and Dry Nitrogen.

Sample	Wt. (mg)	Conditions: Stand. Sample Crucible	Conditions: Rate (°C/min)	Conditions: Atm. (dry)	Exotherm I: Start. Temp. (°C)	Exotherm I: Peak Temp. (°C)	Exotherm I: End Temp. (°C)	Wt. Loss: Peak (% orig.)	Wt. Loss: End (% orig.)
PAN	52.5	Al_2O_3	8	Air	210	295	308	29	34
PAN	68.5	None	2	Air	208	265	281	9	24
20	70.0	Al_2O_3	4	Air	244	340	-	33	-
20	70.2	Al_2O_3	8	Air	255	350	-	46	-
PAN	44.0	Al_2O_3	8	N_2	225	285	330	11	20
PAN	86.9	None	2	N_2	230	278	281	6	8
20	62.8	Al_2O_3	8	N_2	295	368	-	54	-

Table 2. DTA/TGA Characteristics of Polyacrylonitrile and Impure 2,4,6,8-Tetracyanononane, 20, in Dry Air and Dry Nitrogen (Continued).

Endotherm			Exotherm II			
Peak (°C)	Wt. Loss to Peak (% orig.)	Start. Temp. (°C)	Peak Temp. (°C)	End Temp. (°C)	Wt. Loss Peak (% orig.)	Wt. Loss End (% orig.)
-	-	415	550	682	66	98
-	-	380	504	590	63	96
372	50	430	471	542	84	94
390	46	445	495	562	87	94
-	-	-	-	510	-	52
-	-	-	-	410	-	37
391	81	-	-	450	-	96

(Table 1) were overlapping, while a change from a dry air to a nitrogen atmosphere had little effect on the curves. The initial exotherm occurred over a range of 220-262°C (peak temperatures) for the 2 models, somewhat lower than that reported for PAN[40, 64, 190-215, 279], and lower than that observed for PAN pyrolyzed in the current investigation (Table 2). The most important difference in the exotherm, however, was that it was extremely weak and broad in all cases, whereas the corresponding transition for PAN is characteristically sharp and intense[279]. As the initial sharp exotherm with PAN has been generally associated with polymerization of the nitriles[40, 279], the DTA/TGA characteristics of pure 18 and 19 indicated that little cyclization was occurring during the course of the exotherm. Small weight losses were recorded to the peak of the exotherm. Such weight decrease has been attributed in PAN pyrolysis to minor chain scission (an endothermic process[214-215]) arising in conjunction with the nitrile polymerization (the exothermic process observed in the DTA/TGA). As the graphs under N_2 varied little from those under air, contribution to the exotherm by oxidative attack at the nitriles was unlikely[176-182]. The absence of significant differences under the 2 atmospheres also denoted that nitrile cyclization was minor, as the broadened exotherm of PAN pyrolyzed in air or O_2 was due to oxidative stabilization of the naphthyridine-type rings[193, 196, 279]. Thus the existence of the weak exotherm in conjunction with the concurrent weight loss and the

independence of the curves of the type atmosphere employed signified that nitrile cyclization was a minor reaction in the heat-treatment of pure 18 and 19.

The only other transition in the DTA/TGA graphs of 18 and 19 was a sharp, intense endotherm that began at the peaks of the exotherms and reached summits at 290-371°C (Table 1). Most of the weight loss had occurred by the peak temperature of the endotherms or shortly thereafter. The appearance of the graphs were similar to the reported DTA/TGA plot of the pyrolysis of polymethacrylonitrile (MAN), where the only major characteristic observed was also a strong endotherm occurring in the range 315-360°C with corresponding catastrophic weight loss[214]. The endotherm was shown to be due to chain scission (radical formation), mainly via unzipping[197, 214, 283]. Hay has shown by DSC/TVA that the strong exotherm in PAN pyrolysis masks a weaker endotherm that continues beyond the exotherm[215]. Chain scission with accompanying weight loss was postulated as the cause of the endotherm. Although high MW polymers are more stable to thermal degradation than corresponding low MW analogs[402], another important factor that merited consideration with 18 and 19 in contrast to PAN was the possibility of volitilization in the endotherm range. Although the boiling points of 18 and 19 were high (185-187°C (0.08 mm) and 156-160°C (0.10 mm), respectively), the compounds were both liquids above 60°C, and thus considerable vapor pressure was expected in the

endotherm peak range due to the large surface area. As seen in Table 1, faster heating rates and smaller samples resulted in lower endotherm peak temperatures and corresponding loss of total weight in comparative tests. In addition, the model 18 showed consistently greater endotherm peak temperatures while retaining sample in the crucible to higher temperatures in comparison to 19. Since 18 had a considerably higher bp than 19, and as chain scission should have been independent of sample weight in rate and would have resulted in formation of some high MW, less-volatile products by radical combination, it appeared that the strong endotherm and coincident drastic loss of weight was mainly due to volatilization of the models under the test conditions.

Questions arose as to possible catalytic effects of the standard, Al_2O_3 (a Lewis acid), on the degradation of the models or polymer. As seen from Tables 1 and 2, the differences between comparative runs with and without Al_2O_3 in the sample crucible were negligible, e.g., the 2 runs of 18 under N_2 in Table 1.

DTA/TGA of PAN and 2,4,6,8-Tetracyanononane (20)

The DTA/TGA graphs of the redox-initiated, slurry-produced PAN polymer (Table 2) were comparable to that reported[180]. The initial exotherm was much sharper and more intense than that observed for the 3-unit models, with higher average weight losses at the peak. Alteration of the heating rate from 8°C/min to 2°C/min lowered the exotherm peak temperature and substantially decreased the weight loss at the peak in

accordance with the observations of earlier workers[40, 197,279]. The peak temperatures under both air and N_2 were the same at 2°C/min, and the corresponding weight losses were comparable, confirming the oxidative stabilization effect obtainable by isothermal heating (slow rate of heating in the present case) of PAN in air[281]. No endotherm was observed in the DTA graph of PAN[215]. In the tests performed under dry air, a second exotherm occurred in the 500-550°C peak-temperature range that was not present in the graph for the N_2-pyrolyzed polymer. As no 18 or 19 had been present at such high temperatures, the exotherm was also absent in the graphs of the 3-unit models. The broad, strong exotherm was apparently due to the complete oxidative destruction of the polymer, as little weight remained after the exotherm, and no carbon was observed in the crucible at the termination of the test. In contrast, considerable weight remained at greater than 400°C in the sample crucibles treated under N_2, and a copius amount of carbon was found in the crucible and instrument oven at the termination of the tests. Thus the importance of carbonizing the PAN under inert atmospheres at higher temperatures was reaffirmed[8-10, 102-110].

The impure 4-unit model, 20, was found to exhibit thermal characteristics similar to both the 3-unit models and PAN (Tables 1 and 2). The initial exotherm was less intense than that of PAN, but significantly stronger than that observed for 18 or 19. The weight loss to the exotherm peak was higher in all cases than that suffered by any of the other systems,

and the peak temperatures were also higher. A strong endotherm immediately followed the exotherm, with temperatures considerably higher than for the corresponding 18 or 19 peaks. The total weight loss at the endotherm peak, however, was much lower than that for the 3-unit models, and considerable weight remained in the tests under air up to 430-445°C. At that point, a second exotherm comparable to that observed for PAN (though not as intense) began, with most of the sample lost by the end of the exotherm. Under N_2, no second exotherm was observed, and a much higher percentage weight loss had occurred by 450°C than with PAN. Some carbon was observed in the sample crucible at the termination of the test.

The more intensive exotherm for impure 20 than for 18 or 19 indicated significantly increased nitrile polymerization in the former, and thus supported the earlier conclusions that β-ketonitrile, amide, acid, or other impurity or comonomer functional groups on the chain of PAN[154-160. 284-287] or its models[333] were necessary for cyclization initiation to occur at a significant rate. The strong endotherm with 33-54% weight loss denoted that volatilization with minor degradation was a major process as with 18 and 19. However, the retaining of significant weight to the second exotherm also supported ring formation, as high MW products formed by inter-chain imine formation[279] (expected to be more prevalent in the liquid state than in the polymer[176-182]) would possess a

lowered tendency to volatilize in comparison with uncyclized 18, 19, or 20.

The increased initial exothermic peak temperature for the run of 20 under N_2 in comparison to those under air was anomalous with both PAN and the 3-unit models. No clear explanation could be devised, though perhaps the impurities in the model in conjunction with increased oxidative stabilization due to the higher surface area in relation to the polymer resulted in a lowered energy of activation for the lini-up, i.e., the process was initiated at lower temperatures in air than in N_2 but with less exothermic character in the former. A higher weight-loss at the exotherm with N_2 also indicated increased fragmentation, although the effect of the higher peak temperature relative to the air experiments on the degree of fragmentation was uncertain.

^{13}C-NMR Analyses of PAN Models

The spectra of the simpler models of PAN (1,3-dicyanopropane and 1,3-dicyanobutane) were collected to facilitate the assignments of the carbons in the more-complicated models (Table 3). The 2,4-dicyanopentane spectra (corresponding to the meso (isotactic PAN model) and racemic (syndiotactic PAN model) stereoisomers) were obtained from the literature[342]. The absorptions of 1,3-dicyanopropane corresponded to the reported values[392], while the assignments for the 1,3-dicyanobutane were made by correlation with the absorptions of 1,3-dicyanopropane and 2,4-dicyanopentane[342].

Table 3. ^{13}C-NMR Absorptions of 1,3,5-Tricyanopentane (18), 2,4,6-Tricyanoheptane (19), and Related Compounds in PPM from TMS.

Compound	$CH_3\underset{*CN}{CH}$	$(CH_2)_2\underset{CN}{CH}$	$\underset{CN}{CH_2}CH_2$	$(CH_2)_2\overset{*}{\underset{CN}{CH}}$
18	-	119.279 (36%)	118.493 (18%)	29.910 (30%)
19	121.585 (33%)	119.464 (49%)	-	36.038[1] (42%)
	121.284 (86%)	-	-	35.492 (22%)
	-	-	-	34.946 (19%)
1,3-Dicyanopropane	-	-	118.672 (86%)	-
1,3-Dicyanobutane	121.468 (67%)	-	118.551 (73%)	-
2,4-Dicyanopentane, Meso[342]	122.86	-	-	-
2,4-Dicyanopentane, Racemic[342]	121.10	-	-	-

*Denotes the carbon whose absorption position is shown in the column.

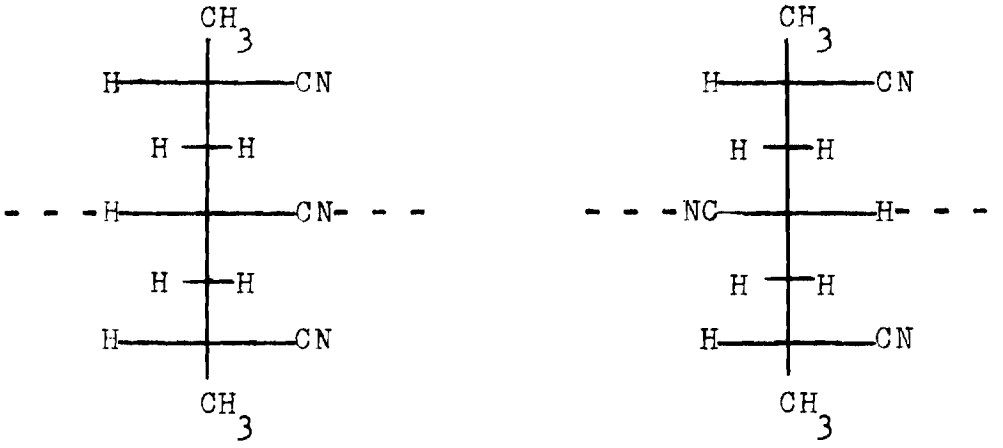
[1]The absorption consisted of 2 merged peaks.

Table 3. ^{13}C-NMR Absorptions of 1,3,5-Tricyanopentane (18), 2,4,6-Tricyanoheptane (19), and Related Compounds in PPM from TMS (Continued).

$(CH_2)_2^*CH_2$ CN	$CH_2^*CH_2CH$ CN CN	$(CH)_2^*CH_2$ CN	$CH_2^*CHCH_2$ CN	$^*CH_3CH$ CN	$^*CH_2CH_2$ CN
-	27.241 (39%)	-	-	-	15.167 (40%)
-	-	28.940 (15%)	24.147 (42%)	18.019 (41%)	-
-	-	28.091 (20%)	23.237 (33%)	17.412 (29%)	-
-	-	26.998 (10%)	-	-	-
21.538 (43%)	-	-	-	-	16.320 (77%)
-	29.365 (55%)	-	24.693 (76%)	17.352 (46%)	15.107 (47%)
-	-	37.80	23.30	17.72	-
-	-	38.46	24.41	18.16	-

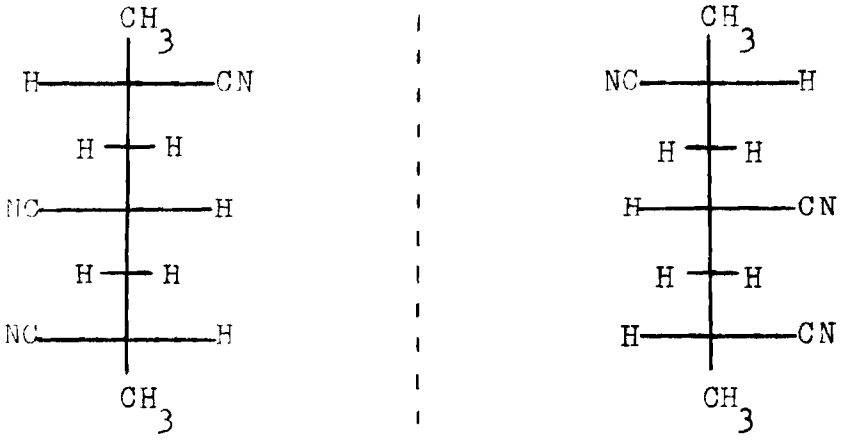
The ^{13}C-nmr spectrum of 1,3,5-tricyanopentane (18) was simple, as no asymmetric carbons existed in the structure. Off-resonance spin-decoupling confirmed the assignments of absorptions to specific carbons by n+1 splitting[387].

The spectrum of 2,4,6-tricyanoheptane (19) was by far the most complicated of the ones examined (Table 3). The complexity resulted from the fact that corresponding carbons of pairs of stereoisomers exhibit slightly different chemical shifts in ^{13}C-nmr[342-343]. As shown in Figure 6, 3 stereoisomers were possible for 19, 2 being meso (corresponding to isotactic and syndiotactic PAN segments) and 1 being racemic (analogous to atactic PAN segments). Two peaks for the end methyls, the methine carbons in the 2- and 6-positions, and the nitriles on the outer carbons indicated that 2 of the possible 3 structures had preferentially formed during the course of the synthesis. In contrast, all 3 stereoisomers had been separated from the stereochemical mixture in the synthesis of 19 by the Takata-Taniyama method[320-321], and the structures characterized by high-resolution ^{1}H-nmr[326-327]. The 3 peaks for the methylene units observed in the ^{13}C-nmr spectra of 19 denoted that the racemic d,l-pair had been 1 of the products formed, as Murano and Yamadero had observed 2 methylenic ^{1}H-nmr absorptions for the analog of atactic PAN due to the "meso" and "racemic" nature of the units located on opposite sides of the central carbon in the structure (Figure 6). As 2 of the 3 methylene absorptions were close to each other (28.940 ppm and 28.091 ppm), they were



Meso-I
(Isotactic)

Meso-II
(Syndiotactic)

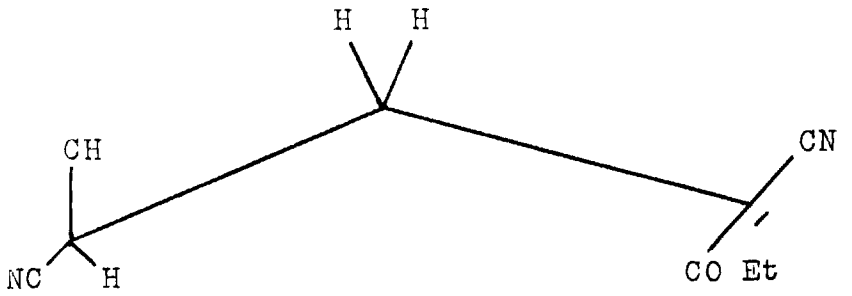


d,l-Pair
(Atactic)

Figure 6. Possible Stereoisomers Produced in the Synthesis of 2,4,6-Tricyanoheptane (19).

designated as the absorptions due to the d,l-pair. The 4 peaks (2 merged) assigned to the central methine carbon of 19 were unexplained; the appearance of the group, however, was somewhat similar to that exhibited by the methine carbon in the ^{13}C-nmr spectra of PAN[339-341]. The reported absorption for the methylene of 2,4-dicyanopentane (the central atom in the molecule)[342] was at a considerably higher ppm than that found for 19, signifying the marked effect obtained by adding a third acrylonitrile unit to the chain and the different environments experienced by a central-atom methylene and off-center methylenes.

No conclusion could be drawn from the spectra alone as to whether the remaining unidentified stereoisomer was of the meso-I or meso-II types (Figure 6). The developed synthesis involved intermediate, sp^2-hybridized (planar) carbanions not generated in the Takata-Taniyama method[320]. For example, whereas the prior workers utilized a Sn2 displacement reaction to form the ester precursor of 19, the presented method utilized a second Michael addition with ethyl-2,4-dicyanopentanoate and methacrylonitrile. The former mechanism is concerted with inversion of configuration at the carbon attacked[403], whereas the latter proceeds via the carbanion 31[357]:



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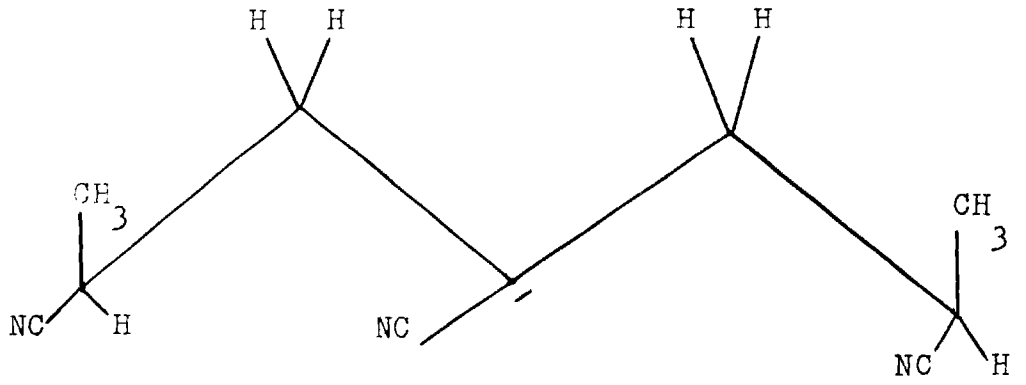
Rotation around the planar carbanion of 31 and each carbanion subsequently formed in the synthesis would occur to minimize steric and electronic interactions between bulky groups in the molecule. The final carbanion in the presented synthesis of 19 was produced in the adapted Krapcho-Lovey decarbalkoxylation of the ester precursor of the model:



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From studies with molecular models of the carbanion 32 and the final product, it appeared that the rotation about the plane before protonation would preferentially lead to the meso-II (syndiotactic model) stereoisomer in a near planar zig-zig arrangement (H ⟷ CN interactions by Newman projections

rather than H⟷H and CN⟷CN interactions down the chain). The d,l-pair (atactic model) could be formed with some minor twisting of the molecule to relieve the steric repulsion between the bulky nitriles. The meso-I configuration (isotactic analog) was highly strained in the completed form without excessive twisting, again due to nitrile interactions, and was eliminated as a logical choice for the unidentified stereoisomer.

Thus the racemic and meso II structures (Figure 6) were rationalized as being produced in the developed synthesis of 19 from the ^{13}C-nmr spectra and molecular model studies. Formation of all 3 stereoisomers by the Takata-Taniyama route[320-321] may have been due to the different character of the transition state in the copper-catalyzed, high-temperature decarboxylation of the acid precursor of the model. No explanation could be devised for the claimed production of optically-active models from optically-inactive starting materials by the Takata group, and none was offered by the previous authors[320-321].

Syntheses of PAN Models, Related Chemistry

Decarbalkoxylation of Reactive Esters

In attempting to promote chloride attack at the carbonyl of semicarbazones with the Krapcho-Lovey decarbalkoxylation reaction system[346], it was discovered that chloride ion was an unnecessary reagent for production of the isolated azine (see the sections concerning the syntheses of azines). Due to the reasons stated in the Introduction, curiosity arose as to

the necessity of the chloride or similar anions in the decarbalkoxylation of reactive esters[345-346]. The results obtained with the reactive esters tested are summarized in Table 4. The yields isolated without NaCl were comparable to those obtained with the salt present[346]. However, the reaction times were considerably longer in 2 of the cases and the corresponding maximum temperatures were lower in comparative runs without NaCl. It was suspected that the longer reaction times were a result of the lower temperatures, which were in turn suspected of being caused by the absence of the colligative property effect afforded by the dissolved salt in the Krapcho-Lovey procedure[346] (Table 4). Such an effect would raise the bp of the pot liquid, and hence speed up the rate of reaction. A decarbethoxylation was thus performed with ethyl phenylmalonate in which the lower-boiling components (H_2O and produced EtOH) were distilled off until a pot temperature comparable to that of the previous workers was reached (146-175°C). A 93% yield of ethyl phenylacetate was obtained in 2 hr (the same reaction time as used previously with NaCl[346]), thus proving the theorized colligative property effect of the salt on the pot temperature and the importance of the final temperature on the rate of reaction.

The necessity of the added H_2O also came into question. The Krapcho group had reported that NaCN-dry DMSO readily decarbalkoxylated reactive geminal diesters[345]. A run performed in the present investigation with ethyl phenylmalonate and dry

Table 4. Results Obtained from the Decarbalkoxylation of Reactive Esters in the Absence of Sodium Chloride, and Comparison with Literature Results in the Presence of Sodium Chloride[346].

Substrate	Product	Temp. Range[1] Observed (w/o NaCl) (°C)	Lit.[346] (w/NaCl) (°C)	Yield Observed (w/o NaCl) (%)	Lit.[346] (w/NaCl) (%)	Time Observed (w/o NaCl) (hr)	Lit.[346] (w/NaCl) (hr)
Diethyl Phenyl-malonate	Ethyl Phenyl-acetate	146-155	135-170	96	90-95	10	2
		146-155	135-170	96	90-95	10	2
Diethyl Phenyl-malonate[2]	Ethyl Phenyl-acetate	178-190	-	78	-	10	-
Diethyl Phenyl-malonate[3]	Ethyl Phenyl-acetate	146-175	-	93	-	2	-
Ethyl Cyano-acetate	Acetonitrile[4]	152-142	135-165	78	85-95	7	2
2-Carbalkoxy-cyclopentanone	Cyclopentanone	120-142	120-150	75	85-95	5	5

[1] [2]Range over which CO_2 evolution was observed.
[3]Run made in dry dimethyl sulfoxide.
[3]Run in which the low-boiling components (H_2O, EtOH) were distilled off.
[4]The literature yield was reported to include EtOH and DMSO, whereas the actual yield by nmr analysis is reported in the present work.

DMSO alone, however, resulted in higher CO_2-evolution temperatures and longer reaction times than for similar (but not the same) reactive esters studied by Krapcho with NaCN[345], but the yeilds of decarbalkoxylated product were comparable. Thus DMSO alone was shown to decarbalkoxylate ethyl phenylmalonate under strenuous conditions.

Of the several mechanisms published for decarbalkoxylation of reactive esters by chloride or related anions in dipolar, aprotic solvents[346, 351-352], all were based on attack of the salt anion as the initial step. As no chloride was present in the work being reported, the Krapcho-Lovey and related Mueller-Siegfried mechanisms were eliminated[346,352]. As no alkyl-substituted products were isolated, a different mechanism than that proposed for decarbalkoxylations of N-carbalkoxypyrazoles (N-alkylpyrazoles produced) was operating in the present system. A probable mechanism for the decarbalkoxylations in H_2O-DMSO is detailed in Figure 7. Hydrogen bonding between the hydrogen of H_2O and the oxygen of DMSO under the reaction conditions is postulated as increasing the nucleophilicity of the H_2O oxygen and thus facilitating the attack on the ester carbonyl. The proposed mechanism accounts for the observed characteristics of the reaction (decarbalkoxylated product, EtOH formed, CO_2 evolved). The seemingly catalytic effect of the chloride ion which had influenced the formulation of the Krapcho mechanism[346] was irrelevant for the 3 substrates examined.

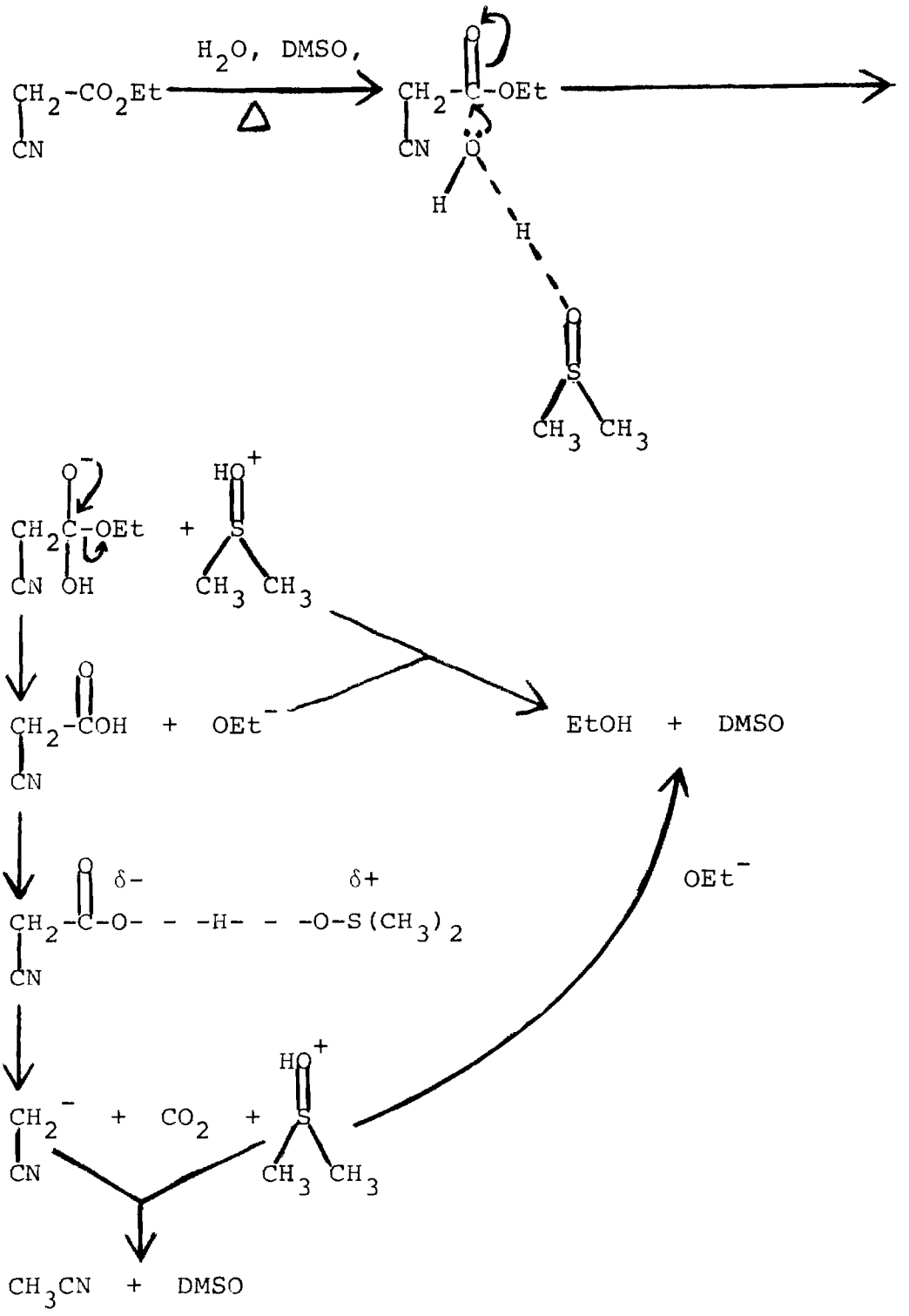


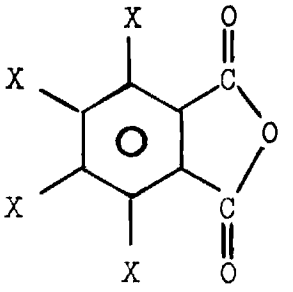
Figure 7. Proposed Mechanism for the Decarbalkoxylation of Reactive Esters in Wet Dimethyl Sulfoxide in the Absence of Sodium Chloride.

In a paper[355] published concurrently with that encompassing the results contained herein[354], Krapcho and coworkers confirmed that NaCl was unnecessary to decarbalkoxylate several reactive esters (including diethyl phenylmalonate) in DMSO-H_2O. Other, less-reactive esters such as diethyl dimethylmalonate, however, required the presence of Cl^- to decarbalkoxylate at a reasonable rate[355]. The significant variation of reaction rate of 2-benzyl-2-carbmethoxycyclopentanone in HMPA with the sodium salt utilized also signified that the anion was taking part in the mechanism for that substrate[352].

Thus for the esters investigated herein and other substrates of similar reactivity[355], the DMSO-accelerated attack of the carbonyl is so rapid (Figure 7) that addition of NaX (X = Cl, Br, CN, etc.) offers little advantage. For less-reactive esters, however, NaX is apparently a necessary component to attain a rapid rate of reaction[352,355]. In the latter case, attack by Cl^- alone (possible greater reactivity[355]) or a combination of Cl^- attack and attack by the partially-formed hydroxide anion is probable. As the relative position of the hydrogen between the oxygens of the H_2O and DMSO (and hence the nucleophilic character of the attacking oxygen) in Figure 7 was uncertain, no definite conclusion could be drawn as to the relative reactivities of X^- and the partially-deprotonated H_2O in the present work.

For the decarbalkoxylation of ethyl phenylmalonate performed in dry DMSO alone, a different mechanism was obviously

operating than that for the wet solvent. Although the decarboxylation of tetrahalophthalic acid had occurred readily in refluxing DMSO[353], it is likely that the mechanism involved the anhydride intermediate 33 instead of the proposed transition state 23 under the reaction conditions[404]:



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The adaptation of the Chen-Yan mechanism[353], however, to the observed decarbalkoxylation in dry DMSO led to the scheme proposed in Figure 8. The reaction path involves abstraction of a methyl hydrogen of low acidity by dimethyl sulfoxide, and thus would require the strenuous conditions utilized in the synthesis. The initiating species may have been 1 or more of the many intermediates (particularly radical-anions) postulated as forming in the complete decompositon of dry DMSO at reflux in air[358] in addition to or instead of the solvent as pictured in Figure 8. No attempt was made to isolate ethylene to support the postulated mechanism, as dehydration of any ethanol formed to C_2H_4 under the reaction conditions was possible.

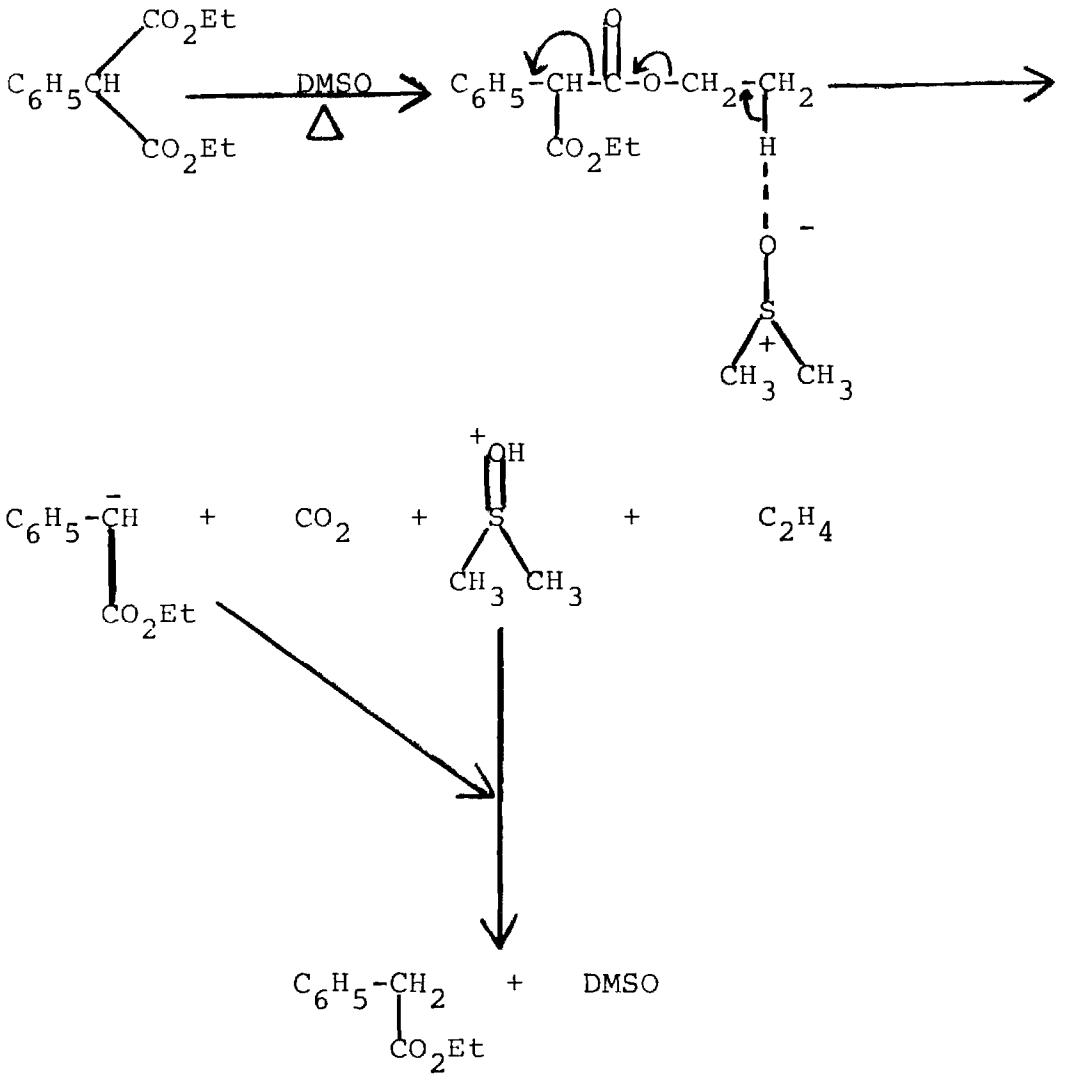


Figure 8. Proposed Mechanism for the Decarbalkoxylation of Ethyl Phenylmalonate in Dry Dimethyl Sulfoxide in the Absence of Sodium Salts.

Syntheses of Azines

The initial interest in the treatment of carbonyl derivatives with the chloride ion of the Krapcho-Lovey system[346] was in promoting attack of the anion on the carbonyl of semicarbazones, and, through a series of eliminations, to produce the alkane derivative, i.e., to perfect a new Wolff-Kishner type reaction. However, work-up of the reaction mixtures led to isolated azines of moderate to good yields. As no mechanism could be devised to explain the azine formation via attack of the Cl^- ion, the reaction was repeated without NaCl with similar results, and thus further investigation of the procedure was initiated.

The details of the results obtained are summarized in Table 5. The only similar example to the author's knowledge in the literature of such a coupling of hydrazones in DMSO was the formation of the azine as a side-product upon treatment of the carbonyl derivatives with potassium tert-butoxide in dry solvent (25°C) to prepare the corresponding alkanes[385]. Inference was that the strong base, not the solvent, was responsible for the coupling[385]. In a related study, Kotchetkov and Vorotnikova isolated azines from acetylhydrazones treated with HCl in refluxing isoamyl alcohol[386]. Formation of the free hydrazone and disproportionation to the azine was postulated, though no reaction mechanism was presented for the latter process[386]. A possible mechanism for the formation of the azine from the hydrazone in the current

Table 5. Syntheses of Azines from Carbonyl Derivatives.

Substrate	Product	Solvent-Reagent	Conditions Temp. Range (^{o}C)	Time (hr)	Recrystal. Yield (%)
Benzaldehyde-semicarbazone	Benzalazine	DMSO-H_2O	150-162[1]	2.5	44
Benzophenone-hydrazone	Benzophenon-azine	DMSO[2]	Reflux	19	51
Benzophenone-hydrazone	Benzophenon-azine	DMSO[2]	25	500	72

[1]Range of CO_2 evolution observed.

[2]Commercial DMSO of undetermined H_2O content that was not dried before use.

study is presented in Figure 9. Of the 2 possible paths, Path b appears to be the most likely route due to Cram's discovery that a rapid rate of butoxide addition to the dry DMSO-hydrazone system dramatically increased the production of azine in lieu of alkane[385]. Thus anion formation by hydrogen abstraction with the strong base was a logical first step in both azine and alkane formation (see structure 27)[385]. Although not as strong a base as the butoxide at 25°C, the DMSO is postulated to abstract the amine hydrogen readily at higher temperatures to initiate the process. Deprotonation of the hydrazone by radical-anions or other thermal decomposition product intermediates of DMSO[358] would also facilitate proton abstractions at higher temperatures. As Paths a and b merge in Figure 9, however, either route would culminate in the azine and hydrazine as products.

As azine was also formed from semicarbazones treated as the hydrazone but with added H_2O, a preliminary reaction as shown in Figure 10 to form the free hydrazone anion is postulated[386], followed by further reaction to the azine as in Figure 9. The decomposition of carbamic acid to CO_2 and NH_3 is known to proceed readily[405], and under the reaction conditions employed break down is pictured as occurring rapidly. Copius amounts of CO_2 were detected by a barium hydroxide trap for the semicarbazone reactions, supporting an unstable intermediate of carbamic acid. No attempt was made to isolate or identify NH_3 or N_2H_4 in the reaction procedure.

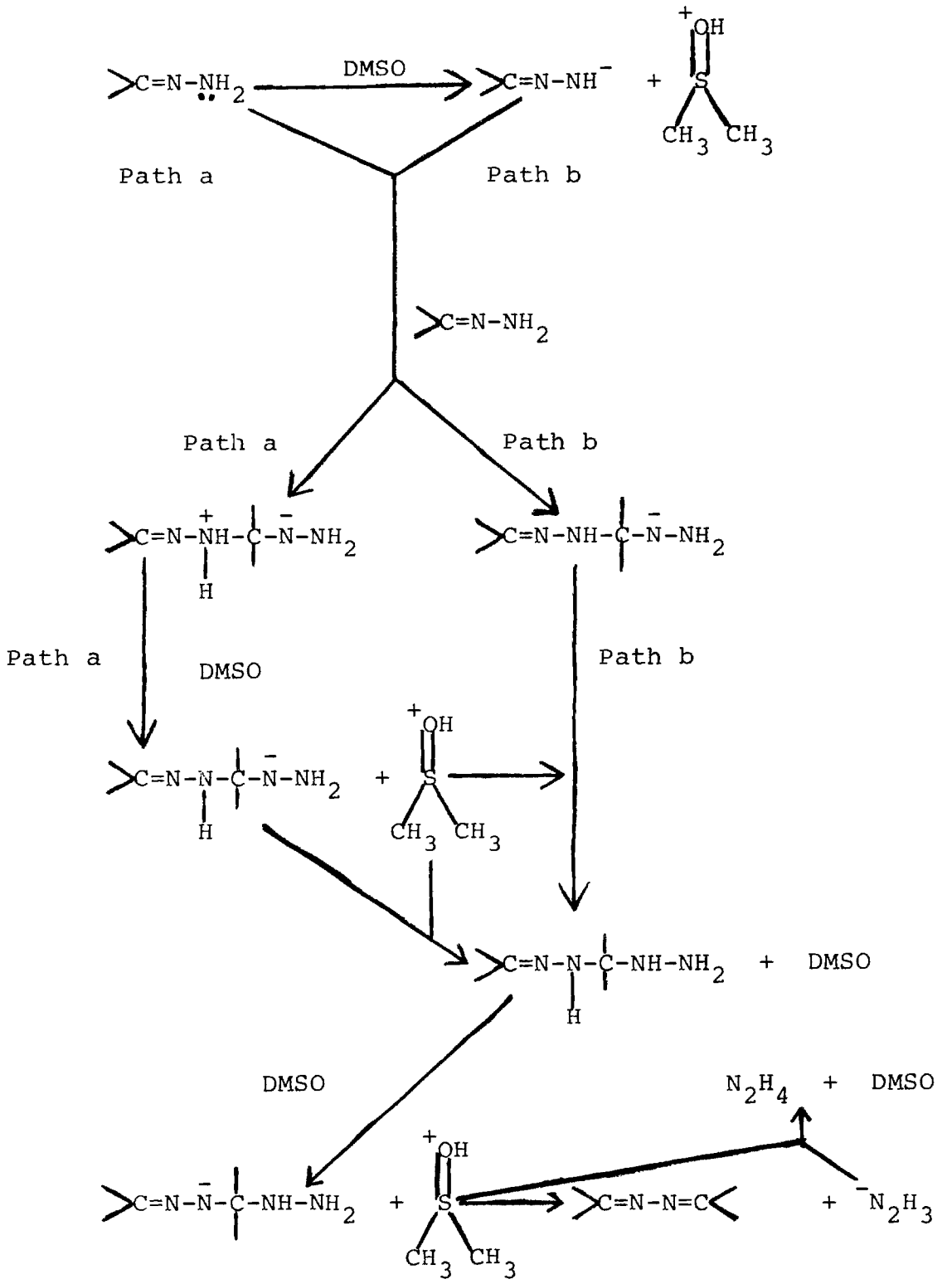


Figure 9. Proposed Mechanism for the Formation of Azines from Hydrazones in Non-anhydrous Dimethyl Sulfoxide.

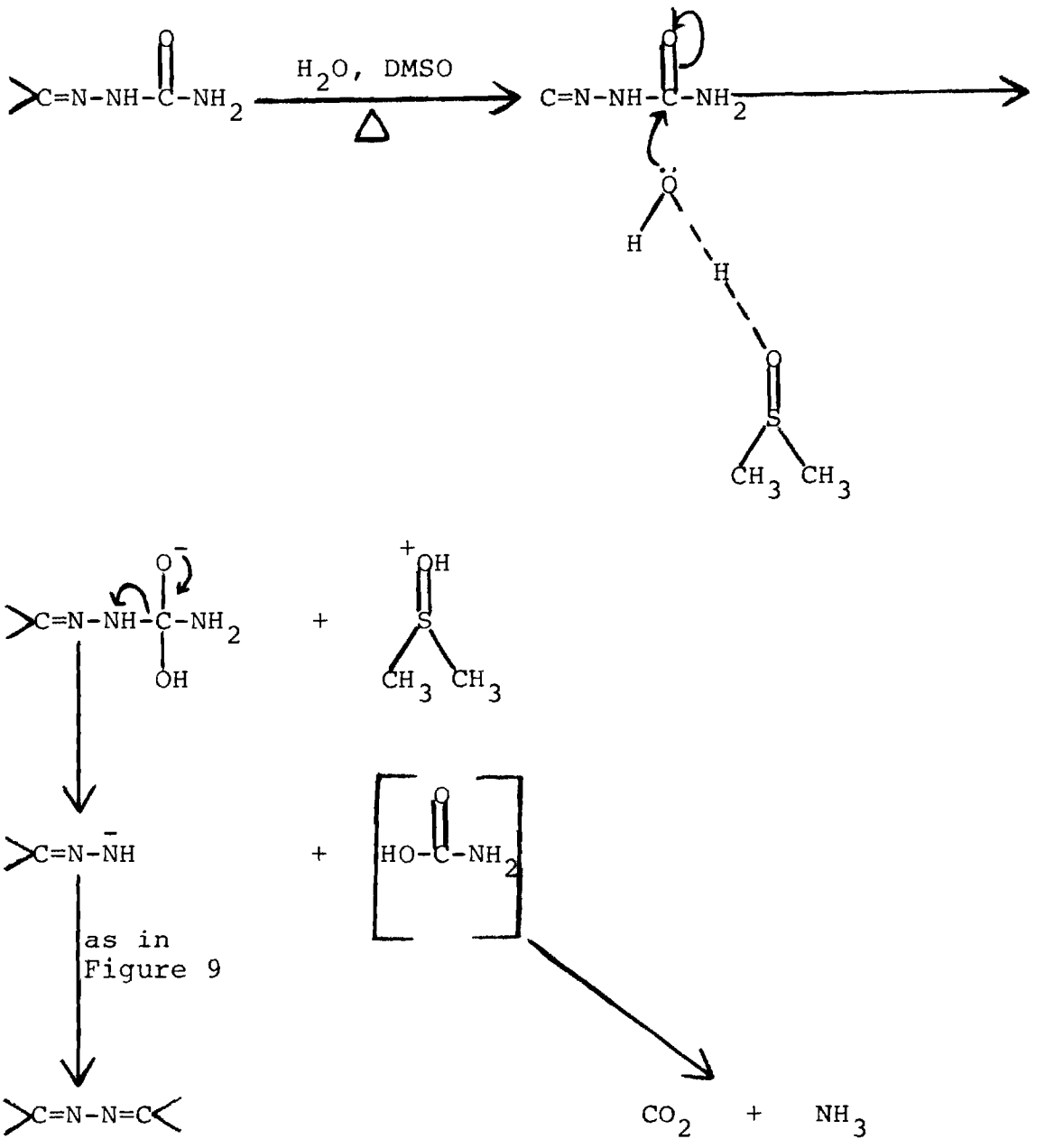


Figure 10. Formation of Free Hydrazone Anion from Semicarbazones in Wet Dimethyl Sulfoxide.

Thus it was shown that carbonyl derivatives such as hydrazones or semicarbazones may be converted in facile fashion to the corresponding azines by simply heating the compounds in DMSO. Although the investigation was not thorough or broad enough to claim a new general preparation of azines, the presented procedure appears to be comparable in mildness, simplicity, and yields to the reported conversions of pre-formed hydrazones to the azines, e.g., by H_2SO_4-catalyzed disproportionation in EtOH[367-368].

CHAPTER IV

CONCLUSIONS, POLYACRYLONITRILE MODELS

Syntheses of PAN Models

Novel procedures are described in this section for synthesizing the pure 3-unit models of PAN, 1,3,5-tricyanopentane (18) and 2,4,6-tricyanoheptane (19). The syntheses are simpler, less strenuous, and result in higher overall yields of product than previously-published methods[317,320]. The main improvement over the older procedures is development of a 1-step, facile decarbalkoxylation of the ester precursors of the models to the alkyl nitriles via the adapted Krapcho-Lovey reaction[346]. The overall yield is limited, however, by the formation of reverse Michael addition product in decarbalkoxylations. Comparative reactions indicated that the initiation step of the reversal involved abstraction of the relevant acidic hydrogen by chloride ion and/or DMSO. The ester precursors were demonstrated not to be exceptionally reactive[355], as NaCl had a beneficial effect on the rate in comparative tests with 18.

In addition, several improvements were made in the preparation of the model ester precursors, 3-carbethoxy-1,3,5-tricyanopentane (new route to cleaner initial product, improved purification technique) and 4-carbethoxy-2,4,6-tricyanoheptane (new route). The strenuous conditions employed by Takata and

Taniyama in the production of the Michael addition monoadduct, ethyl-2,4-dicyanopentanoate, were found to be necessary to isolate a high yield of the product[320]. Attempted preparation of ethyl-2,4-dicyanobutanoate by reaction of ethyl cyanoacetate anion with acrylonitrile was unsuccessful.

An improved synthesis of crude 2,4,6,8-tetracyanononane (20) is also detailed (higher overall yield, greater simplicity)[320]. However, attainment of the pure model was not achieved, with identified impurities similar in nature to those present in the material produced by the Takata-Taniyama method[320].

DTA/TGA Analyses of PAN and its Models

In the DTA/TGA of pure 1,3,5-tricyanopentane (18) and 2,4,6-tricyanoheptane (19), only a broad, weak exotherm with minor weight loss was recorded in the temperature region where PAN gives the characteristic strong, sharp exotherm[279]. Little change was noted in the DTA/TGA of 18 and 19 under N_2 or air, denoting that contribution to the exotherm by oxidative attack at the nitriles was negligible[176-182]. The weak exotherm was due to minor cyclization, and the corresponding weight loss to minor chain scission and/or volatilization. The main characteristic of the DTA/TGA was a sharp, strong endotherm that directly followed the exotherm and that was accompanied by almost total loss of weight by 360°C. The endotherm was absent in the DTA/TGA of PAN, and was attributed mainly to volatilization of the low-MW models with minor chain

scission. Use of Al_2O_3 as a standard in the sample crucible was determined to have negligible effects on the thermal characteristics of the models and PAN.

Thus the pure 3-unit models were shown to be inadequate models for the thermal behavior of PAN. The lack of significant nitrile cyclization dictated that the Grassie self-initiation mechanism[66] (see structures 9 and 23) was improbable, and the observed volatilization-fragmentation at relatively low temperatures indicated that the failure of Takata to observe uv peaks due to self-initiated, cyclized product in the thermal degradation of 19 (200-300°C, sealed tube) was probably a result of vaporized sample[334].

The DTA/TGA characteristics of redox-initiated, slurry produced PAN were comparable to those reported[180]. In air, near-complete weight loss during a second exotherm (500-550°C) was due to total oxidative breakdown of the polymer. In contrast, a high carbon yield resulted under N_2.

The 2,4,6,8-tetracyanononane (20) prepared by the Takata-Taniyama route[320] exhibited thermal characteristics similar to both the 3-unit models and PAN. A moderately-intense initial exotherm, retainment of considerable weight after the following endotherm, and appearance of a second exotherm under air all indicated that more extensive cyclization had occurred with impure 20 than for pure 18 or 19. Some carbon was isolated from heat-treatment of 20 in N_2. Thus the conclusion of earlier workers that impurity or comonomer

functional groups on the chain of PAN[154-160, 284-387] were necessary for significant nitrile cyclization to occur was confirmed. Reasonable correlations of the thermal characteristics of the impure model and PAN could thus be drawn, and it is concluded from the overall results that impurities are necessary components of PAN models to be utilized in thermal comparison tests with the polymer.

^{13}C-NMR Analyses of PAN Models

By correlation of the ^{13}C-nmr absorptions of simpler PAN models (1,3-dicyanopropane, 1,3-dicyanobutane, and 2,4-dicyanopentane[342]) with those of 1,3,5-tricyanopentane (18) and 2,4,6-tricyanoheptane (19), assignments for the carbons of the 3-unit models were made for the first time. Off-resonance spin-decoupling was utilized to confirm assignments for 18, which exhibited a simple spectra (no asymmetric carbons). The spectra of 19 was complex due to the presence of stereoisomers[342-343]. Two peaks for the end methyls and several other carbons in the structure revealed that 2 of the possible 3 stereoisomers were present in the mixture. Three peaks for the methylene carbons (2 close together) identified 1 of the stereoisomers as the d,l-pair (atactic model)[327]. From molecular model studies of the carbanion intermediates formed along the reaction path and the relative stabilities of the final products, the meso-II (syndiotactic model, Figure 6) was postulated to be the second stereoisomer preferentially produced in the synthesis of 19. Although the 4 absorptions (2 merged)

for the central methine carbon of 19 could not be explained, the appearance of the absorption band was somewhat similar to that exhibited by the corresponding carbon in PAN[339-341]. No explanation could be devised for the reported production of optically-active models from optically-inactive starting materials by the Takata group[320-321].

Syntheses of PAN Models, Related Chemistry

Decarbalkoxylation of Reactive Esters

It was shown that for reactive geminal, β-keto, and α-cyano esters, NaCl is an unnecessary component in the wet DMSO decarbalkoxylation procedure of Krapcho and Lovey[346]. Longer reaction times without NaCl were shown to be caused by absence of the colligative effect of the dissolved salt incorporated in the Krapcho-Lovey system[346], e.g., by distilling off the low-boiling components to achieve higher pot temperatures and corresponding faster rates of reaction. A mechanism was formulated for decarbalkoxylations in wet DMSO involving solvent-assisted attack of hydroxide ion on the ester carbonyl to eliminate ethoxide ion and form the carboxylic acid, followed by DMSO-assisted elimination of CO_2 and generation of the alkane (S_E1-type elimination[406], Figure 7). Decarbalkoxylation rate dependence of several unreactive esters on the presence of NaCl[355] or the type of sodium salt utilized[352] indicated that the salt anions were taking part in the mechanism for the conversion of the more-stable substrates, alone or simultaneously with attack by the partially-formed hydroxide ion postulated herein.

Ethyl phenylmalonate was also demonstrated to decarbalkoxylate in good yield in dry DMSO alone at higher temperatures, indicating NaCN[345] to be an unnecessary reagent. For the dry system, a DMSO-assisted fragmentation mechanism to produce CO_2, C_2H_4, and the alkane was devised (Figure 8).

The decarbalkoxylation results contained herein have been published[354]. Part of the studies have been successfully repeated by other authors, and the investigation of the necessity of the salt anion in the wet DMSO broadened[355].

Syntheses of Azines

Benzophenone hydrazone yielded the azine when heated in commercial-grade DMSO at reflux or at room temperature. Benzaldehyde semicarbazone was also converted to the corresponding azine in good yield in wet DMSO alone at 150-162°C. For the former reaction, a mechanism involving attack of the amine nitrogen (either the neutral nucleophile or the amine anion) on a second hydrazone carbon was formulated, followed by elimination of hydrazine to produce the azine (Figure 9). Attack of the semicarbazone by DMSO-assisted, partially-formed hydroxide ion was postulated as producing unstable carbamic acid (subsequently decomposing to CO_2 and NH_3) and the anion of the free hydrazone, which further reacted to give azine (Figure 10).

Although the investigation was not thorough or broad enough to claim a new general preparative procedure for azines, the limited results indicated the method was comparable to earlier syntheses from hydrazones[367-368]. One advantage was the avoidence of strong mineral acid catalysts[367-368].

CHAPTER V

RECOMMENDATIONS, POLYACRYLONITRILE MODELS

Syntheses of PAN Models

The main potential for improvement in the presented syntheses is in production of pure 2,4,6,8-tetracyanononane (20). Further investigation into the purification of the diester precursor, 4,6-dicarbethoxy-2,4,6,8-tetracyanononane, is needed initially to improve the final product, as the contaminants are carried along in the developed synthesis. Also, the extent of reverse Michael addition occurring in the preparation of 20 has not been determined.

For the 2 3-unit models, 1,3,5-tricyanopentane (18) and 2,4,6-tricyanoheptane (19), future efforts are required to eliminate or reduce the formation of reverse Michael addition products. Two approaches are lowered reaction temperatures and a study of the effectiveness of sodium anions other than chloride in promoting decarbalkoxylation (increased nucleophilic character) while inhibiting the hydrogen abstraction that initiates the Michael addition reversal (decreased base character). Preparation of the unmethylated 4-unit model, 1,3,5,7-tetracyanoheptane, utilizing the reported syntheses of the diester precursor[317,329] and the adapted decarbalkoxylation procedure developed herein, would also be constructive.

DTA/TGA Analyses of PAN Models

The impure 3-unit models 18 and 19 should be prepared by the reported methods[317,320] and their DTA/TGA characteristics compared to the results obtained with the pure models. Comparisons of the DTA/TGA of pure 20 and pure 1,3,5,7-tetracyanoheptane (if preparable) with the impure 4-unit models are needed.

The DTA/TGA of the models should be coupled with TVA analyses[215] to better characterize the observed endothermic process, i.e., to definitely distinguish between volatilization and fragmentation. Isolation, separation, and complete characterization of non-volatile products formed on thermal degradation of the models would expand the knowledge of PAN pyrolysis mechanisms. Base-produced cyclized models should be prepared, and products obtained on oxidation characterized to decipher what role oxygen plays in the stabilization of cyclized PAN. Thermal degradation studies of the copolymer models of PAN[322] using modern analytical tools are also needed.

^{13}C-NMR Analyses of PAN Models

^{13}C-nmr analysis of the stereoisomer mixture of 19 produced by the Takata-Taniyama method[320] should be conducted and compared with that of the model synthesized by the presented method. Separations of the products obtained by both methods into their stereoisomer components[321,342] are needed, followed by complete characterization (including ^{13}C-nmr) of the individual structures. Such an investigation

would unambiguously identify which meso structure is produced in the developed synthesis of 19. In light of Takata's claims[321], investigation of any optical activity possessed by the separated stereoisomers should also be conducted.

Syntheses of PAN Models, Related Chemistry

Decarbalkoxylation of Reactive Esters

Further work is required to clarify the postulated mechanism in the decarbalkoxylation of reactive esters in wet or dry DMSO alone. For wet DMSO, use of H_2O^{18} or D_2O would shed light on the validity of the suggested mechanism (Figure 7). In the dry system, substitution of less-reactive functional groups, e.g., C_2F_5 for C_2H_5 on the diester, should slow down the rate of decarbalkoxylation if the mechanism pictured in Figure 8 is operating. α-Cyano and β-keto esters, as well as geminal diesters other than eithyl phenylacetate, should be tested in dry DMSO to determine if the procedure is general for reactive esters.

The exact role of sodium anions in the decarbalkoxylation of less-reactive esters also needs to be thoroughly examined[352,355]. Decarbalkoxylation of 2-benzyl-2-carbethoxycyclopentane in HMPA alone should be attempted, and the results compared with those reported in the presence of sodium anions[352]. The claim that the reaction in the presence of NaCl is heterogeneous should also be investigated[355].

Syntheses of Azines

A wide range of hydrazones require testing in wet DMSO

before a new, general preparative procedure for azines can be claimed. Conditions also need to be optimized in order to gain the highest yield of azine in the shortest possible time. Other uses of the wet DMSO procedure, e.g., formation of polyazines from dihydrazones, should be investigated. The effect of eliminating added H_2O from the semicarbazone systems warrants evaluation. Other dipolar, aprotic solvents may prove better than DMSO in effecting the reaction. Isolation of N_2H_4 for the hydrazone reaction, and of both NH_3 and N_2H_4 in the semicarbazone reaction is required to support the proposed mechanisms (Figures 9 and 10).

CHAPTER VI

INTRODUCTION, CROWN ETHERS

Historical Background, Cationic Complexing Agents

Introduction

Literally hundreds of powerful cationic complexing agents have been prepared in the past 25 years, with a new family of compounds, synthetic multidentate macrocycles, affording the greatest success. The purpose of this section is to give the reader a thorough literature background, with only brief descriptions, of synthetic multidentate compounds that have been produced and their properties. The main emphasis will be placed on macrocycles, with special stress on macrocyclic polyethers.

Macrocyclic Polyethers

Initial Discoveries. Although macrocyclic polyethers had been synthesized and reported prior to 1967[1-2], their ability to complex metal ions was not recognized. C. J. Pedersen, while synthesizing bis 2-(o-hydroxyphenoxy)ethyl ether from bis (2-chloroethyl) ether and the sodium salt of 2-(o-hydroxyphenoxy) tetrahydropyran containing residual catechol, isolated a small quantity (0.4% yield) of white, fibrous crystals of unknown structure[3]. Pedersen found that the compound was only slightly soluble in methanol; however, when sodium hydroxide was

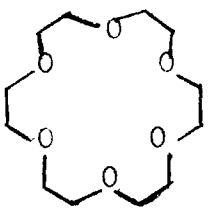
added to the methanol to assess the alkaline effect on the ultraviolet spectra of the material, it was discovered that the fibrous crystals were easily solubilized in spite of the absence of a free phenolic group[3-9]. Further experiments revealed that any soluble sodium salt increased the solubility of the compound in methanol, i.e., the increased solubility was due to the sodium ion and not alkalinity[3,9]. Elemental analysis, nmr analysis, and molecular weight studies identified the by-product as 2,3,11,12-dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene[5]. Pedersen realized that the sodium ion was apparently being held in the center of the cyclic molecule by electrostatic attraction between the positive charge of the sodium cation and the reinforced negative dipolar charge of the 6 oxygen atoms symmetrically arranged around it. With his curiosity aroused by this initial discovery, Pedersen went on to synthesize more than sixty macrocyclic polyethers by condensation methods[3-9]. Since relatively high yields of the large rings were obtained without use of high-dilution techniques, Pedersen concluded that the ring-closing step in the syntheses of crown ethers was facilitated by the cation of the base utilized. In other words, the cation literally "wrapped" the substrates around itself via ion-dipole interaction, and thus brought the reactive functionalities close enough together to increase the rate of ring-closing condensation with respect to cyclization (later termed a "template effect"[14-15]).

Pedersen reported that a large variety of alkali, alkaline earth, and other metal cations formed stable complexes with the neutral macrocyclic polyethers in non-polar aprotic and protic solvents. Many of these complexes were isolated as sharp-melting crystals with melting points far higher than those of the parent macrocycles and with stoichiometries of 1:1 (most prevalent), 2:1, or 3:2 (polyether:salt (mole/mole))[3-9].

Following the work of Pedersen in pioneering the field of macrocyclic polyether chemistry, a tremendous number of publications have appeared concerning these unique compounds. Several partial reviews on the preparation and properties of macrocyclic ligands have been published[16-22].

Nomenclature. The IUPAC rules for bridged hydrocarbons (rules A-31 and A-32) and fused polycyclic compounds (rules A-21 to A-23) give unequivocal but extremely complicated names for the macrocyclic polyethers[3]. Pedersen thus devised a system of ad hoc names particularly for these chemicals[5]. The epithet "crown" was applied to the class of macrocyclic polyethers, with the informal names consisting of (in order): (1) the number and kind of hydrocarbon rings, where applicable; (2) the total number of atoms in the polyether ring; (3) the class name (always "crown"); and (4) the number of oxygen atoms contained in the polyether ring[5]. Symmetrical placement of the hydrocarbon rings (if applicable) and oxygen atoms around the ring is desired if possible. As

pointed out by Pedersen, the simple "crown" names are not unambiguous, and thus should be used only in conjunction with formulas or the IUPAC names. For example, the crown ethers examined in this study are 1,4,7,10,13,16-hexaoxacyclooctadecane (18-crown-6, 1), 1,4,7,10-tetraoxacyclododecane (12-crown-4, 2), and 1,4,8,11-tetraoxacyclotetradecane (14-crown-4, 3):



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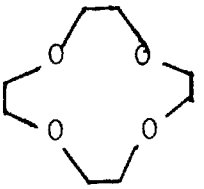

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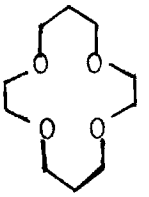

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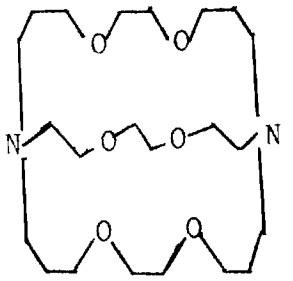
Related Multidentate Compounds

Cryptates. Cryptates are macropolycyclic (usually bi- or tri-cyclic) polyaza-polyoxa compounds that act as ligands for the formation of selective inclusion complexes with various metal cations[16-23]. The cation is surrounded by the 3-dimensional structure, rather than merely encircled as in the crown complexes, and thus is less accessible to anion and solvent[16]. An example of a cryptate is 4:



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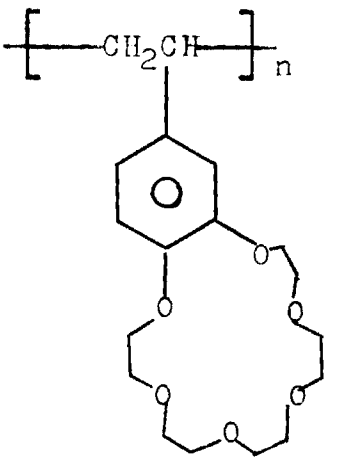
Due to the rigidity of the cryptates in relation to the flexible crowns, the macropolycyclics provide a higher cation selectivity and complex stability[16,22]. Lehn, Dietrich, and Sauvage have pioneered the field of cryptate chemistry in much the same manner that Pedersen pioneered crown ether chemistry[24-25]. Through their efforts, the incorporation of ether linkages in place of methylene groups in macrobicyclic diamines was first achieved[24]. The syntheses, similar to those for the crowns, involve multi-step condensation reactions. Since the initial publication, numerous articles have been published by the Lehn and Dietrich group and others detailing the syntheses, complexing abilities, and utilizations of a wide variety of cryptates[25-38], as well as X-ray structure elucidation of some of the cationic inclusion complexes[39-47]. Interesting recent reports detail the formation of cryptate-alkali metal solutions (useful as reducing agents), and the employments of cryptates in anionic polymerizations. The main hindrance to a wider utilization of cryptates has been the multi-step sequence of reactions required to synthesize the compounds[24], and their resulting high commercial cost.

Crown Polymers. Kopolow, Hogen Esch, Smid, and coworkers recently revealed an elegant class of complexing agents consisting of polymers containing macrocyclic polyethers as pendent groups[48-53]. A typical poly(vinyl crown ether) is poly(vinylbenzo-18-crown-6) with repeating unit 5[48]:



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After resolving the problems involved in synthesizing the crown ether monomers with a vinyl groups attached to the phenyl rings, e.g., vinylbenzo-18-crown-6, the polymers were formed via radical polymerization (toluene or benzene, azobisisobutyronitrile initiator, 70°C) or anionic polymerization (tetrahydrofuran, sodium α-methylstyrene tetramer solution, -80°C). Cation binding studies showed that the crown polymers extracted salts from aqueous solution more efficiently and formed more stable complexes with cations (especially those which have diameters larger than the crown cavity and form 2:1 crown-cation complexes) than the monomers, and exhibited a greater tendency for complex formation with fluorenyl-metal ion pairs[48-53].

In another recent publication related to polymerization and crown ethers, Karagounis and coworkers synthesized intriguing polymers catenanes by reaction of monolayers of

long-chain diacids, e.g., tetradecanedioic acid, with diamines, e.g., 1,12-dodecanediamine, in the presence of dibenzo-60-crown-6[54]. Similar results were obtained in the presence of macrocyclic cyclosiloxanes.

Linear Ethers. Chan, Wong, and Smid reported that polyglycol dimethyl ethers (glymes) formed weak complexes with cations in solution[55]. Although crystalline complexes of the alkali metal salts with linear ethers are uncommon, a few have been reported, e.g., $Na(CH_2O(CH_2CH_2O)_2CH_3)_2$ - $Ta(CO)_6$ by Cotton and Wilkinson[56]. Fenton, Parker, and Wright were able to prepare and isolate high-melting crystalline complexes of poly(ethylene oxide) with several sodium, potassium, and lithium salts[57]. They postulated that the size of the cation may be a critical factor in formation of complexes with poly(ethylene oxide).

Aza, Thia, and Mixed Crowns. Following Pedersen's discoveries with the oxa crowns, interest arose or was restimulated in the syntheses and complexing abilities of macrocycles containing other electronegative atoms. One of the earliest classes of macroheterocycles recognized as complexing agents were the aza crowns (originally called "cyclams")[58-72]. Various aza crowns have been shown to complex successfully Ni(II)[60-71], Ni(III)[70], Co(II)[63], Co(III)[60,63], and Cu(II)[71-72]. A much-improved synthesis of aza crowns (9-21 membered rings, 3-7 heteroatoms, 40-90% yields) has recently been devised[68]. Also, an experimental-theoretical study has been performed

on the relationship of metal-donor distance and ring size in the aza crown-metal ion (Ni(II) and Co(III)) complexes[68].

A report by Ochrymowycz, Mak, and Michner has detailed novel improved syntheses of crowns containing sulfur as the sole heteroatom (thia crowns)[73]. Only a limited number of macrocyclic polythiaethers have been previously reported[74-79]. The syntheses (6-42 membered rings, 2-6 heteroatoms, 0.8-35% yields) involved condensation reactions between dimercapto-alkanes and dihaloalkanes in the presence of base (alcoholic or aqueous solvents)[73].

Syntheses of mixed crowns have also been published, including aza-oxa[10,68,80-84], thia-oxa[10,74,84-90], aza-thia-oxa[26,74,90-91], and aza-thia[15,26,77,92-97] macroheterocycles. In addition, aza-thia-oxa cryptates have been produced[26,98-99]. The synthetic procedures utilized for both mixed crowns and mixed cryptates were similar to those used for the oxa crowns[5-8] and aza-oxa cryptates[24], i.e., they consisted of common condensation reactions.

As a general rule, although complexes are formed with the mixed crowns, substitution of nitrogen or sulfur for oxygen in the crown ring reduces affinity for alkali cations; complexing of Ag(I) ions, however, is either increased or unaffected[3,84-85]. An excellent detailed literature review of synthetic multidentate ligands, including oxa, aza, thia, and mixed crowns and cryptates, along with their complexing abilities, has recently been published[19].

Syntheses of Crown Ethers

Introduction

Following Pedersen's initial reports of crown ether syntheses[4-10], other workers developed synthetic approaches to the oxa macrocyclic complexing agents[14,48-52,101-137]. The most powerful cationic complexing agents (and hence the most useful and interesting from a synthetic utilization viewpoint) in the class of crown ethers appeared to be the unsubstituted 18-crown-6 (potassium ion)[7,84], 12-crown-4 (lithium ion)[120], and 14-crown-4 (postulated, lithium ion)[132]. This section will thus review the literature reports on the various syntheses of crown ethers.

1,4,7,10,13,16-Hexaoxacyclooctadecane (18-Crown-6)

Numerous syntheses of substituted 18-crown-6 have appeared, including those for 1,2-benzo[5], 1,2-4-methylbenzo[14], 1,2-tert-butylbenzo[5], dibenzo (1,2,3,4- and 1,2,5,6-)[5-6], 1,1,5,6-dibutylbenzo, naphtho derivatives[5], and several hydrogenated derivatives[5-6,8,19,100]. The preparation of unsubstituted 18-crown-6 was first reported by Pedersen, who synthesized the compound from 17-chloro-3,6,9,12,15-pentaoxaheptadecanol (hexaethylene glycol chloride) using either potassium tert-butoxide or sodium hydroxide in 1,2-dimethoxyethane[5]. Work-up gave a 1.8% yield of 18-crown-6. Deficiencies of the synthesis were the commercial unavailability of the substrate, the necessity for anhydrous conditions, the necessity of using column chromatography for isolation of the free crown, and an extremely

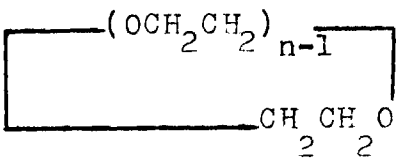
low yield. Initial and subsequent studies revealed that 18-crown-6 complexes potassium ions more effectively than its substituted analogs[5,7,14-15,84]. Dale and Kristiansen published an improved synthesis of 18-crown-6 in which they employed triethylene glycol and the corresponding ditosylate (commercially available) in refluxing benzene with potassium tert-butoxide (33% isolated yield)[101-102]. The product could not be liberated from the complex by simple distillation (the anion apparently attacking the ring). The synthesis thus suffered from the same deficiencies as the Pedersen preparation, although the yield was markedly improved. In a similar study, Greene utilized the starting materials of Dale and Kristiansen, but examined a number of different solvents[14,103]. The 18-crown-6 was isolated in yields of 84%, 30-60%, and 93% in dimethyl sulfoxide (DMSO), tetrahydrofuran (THF), and dimethoxyethane (DME), respectively. However, THF was the preferred solvent from a simplicity viewpoint, and the procedure employing THF was the one detailed[14]. Purification was by "sublimation" (actually a modified distillation performed in a sublimation apparatus, 80°C at 0.01 mm (mp of pure 18-crown-6, 36.5-38°C)) or recrystallization from hexane. The imperfections of the Pedersen synthesis were not corrected, however, with an improved yield the only major improvement. Gokel and Cram developed the first synthesis of crude 18-crown-6 that incorporated commercially available substrates (triethylene glycol and 3,6-dioxa-1,8-dichlorooctane), wet reaction conditions (aqueous KOH-THF), and

simplicity of reaction procedure and work-up including distillation)[104-105]. The method lacked an efficient purification procedure, referring to Greene's difficult sublimation technique (hard to repeat, time consuming, limited quantities), and was not published as submitted. It remained for H. P. Harris and C. L. Liotta to find that 18-crown-6 formed a high-melting, crystalline complex with acetonitrile, and that the complex could be utilized to obtain large quantities of pure 18-crown-6 for the first time[106-107]. The preparation and purification of 18-crown-6 (in which the author played a minor role) has since been reported jointly by the research groups of D. J. Cram and C. L. Liotta[108-109].

1,4,7,10-Tetraoxacyclodocecane (12-Crown-4)

Syntheses of substituted derivatives of 12-crown-4[5,110-112] and unsubstituted analogues containing 1 or more heteroatoms other than oxygen in the crown ring[64,68,73,83,88] have been reported. Few researchers, however, have synthesized the unsubstituted 12-crown-4 cyclic polyether. Stewart, Waddan, and Borrows isolated the material as a minor by-product in the triethyl aluminum acid-catalyzed polymerization of ethylene oxide, and published basic physical data on its structure[113]. Berg, Hermann, and Rehling made a similar discovery in a study of cyclic oligomers obtained from polymerizations[114]. Using the Stewart, Waddan, Borrows method (or a modification thereof[115]) of preparing 12-crown-4, it has been found that the compound causes atrophy of the reproductive glands in

male rats (inhalation exposure)[116], and forms a 2:1 (crown: salt) pentahydrate complex with sodium chloride[117]. Dale, Borgen, and coworkers also synthesized 12-crown-4 by acid-catalyzed cyclic tetramerization of 12-crown-4, and reported additional physical evidence (ir, ^{1}H-nmr, ^{13}C-nmr) of the structure[118-121]. A BF_3-dry HF-dioxane system (room temperature, atmospheric pressure, 18 hr) gave the highest ratio of cyclic products to linear oligomers. The catalyst was destroyed with gaseous NH_3, and the macrocyclic products distilled away from the polymers in wide-boiling fractions. The product distribution as determined by glc was complex, with the following proportions of cyclic oligomers reported[119]:



n:	2	3	4	5	6	7	8	9	10	11	Higher
%:	40	1	15	5	4	3	2	2	1	1	25

The authors postulated that the product distribution was determined by the balancing rates of oligomerization and of degradation of the products to dioxane, both dependent on the ethylene oxide concentration[119]. The only attempt to produce 12-crown-4 by modified Williamson synthesis was made by Dale and Kristiansen using diethylene glycol and its tosylate as substrates with potassium tert-butoxide in refluxing benzene[101-102]. The authors, however, isolated 24-crown-8 as the only cyclic product[101-102].

1,4,8,11-Tetraoxacyclotetradecane (14-Crown-4)

As with the 12-crown-4, several groups have published syntheses of substituted 14-crown-4[5,19,123] and of analogues containing all nitrogen[58-73] or sulfur[73] heteroatoms in the ring instead of oxygen. In addition, the totally-symmetrical 16-crown-4[124] and one of its substituted derivatives[125-126] have been prepared, and their lithium complexing abilities examined[125-128]. Although synthesis of an unsymmetrical positional isomer of unsubstituted 14-crown-4, 1,3,8,10-tetraoxacyclotetradecane, has been devised[129] and the X-ray crystal structure elucidated[130], to the author's knowledge no method of producing unsubstituted 1,4,8,11-tetraoxacyclotetradecane has appeared in the literature[19].

Objectives of Research

18-Crown-6. As unsubstituted 18-crown-6 has been shown to be the optimum crown for complexation of potassium ions[7,84], and as the older synthetic procedures for the compound possessed several undesirable features[5,14,102], the value of a simple, straightforward method to produce pure 18-crown-6 in large quantities from commercially available substrates was of tremendous importance to organic chemistry[108]. Initial developments in the new improved synthesis and purification of 18-crown-6 were made by G. W. Gokel[105] and H. P. Harris[106]. The author's contribution to the reported procedure[108-109] was, therefore, to assist Dr. Harris in improving and perfecting the method of preparing pure 18-crown-6.

12-Crown-4. Based upon work reported for substituted derivatives[5,11] and the crown itself[120], 12-crown-4 appears to be a good complexing agent for lithium cation. Anet, Dale, and coworkers prepared a crystalline 1:1 complex of 12-crown-4 with several lithium salts[120]. The cyclic tetramer of ethylene oxide can be produced by acid-catalyzed methods[113-119], but the approach has several disadvantages, including use of a gaseous monomer, competing formation of other cyclic products[113,119,122], competing linear polymerization[113], and use of expensive, flammable organometallic catalysts[113]. An objective of this project was thus to develop a modified Williamson ether synthesis of 12-crown-4, using commercially available starting materials, wet reaction conditions, and simple reaction and work-up procedures. The results of the research have recently been published[131].

14-Crown-4. From work with Corey-Pauling-Koltun and Fisher-Hirschfelder-Taylor atomic models, Pedersen estimated the cavity diameter of 14-crown-4 to be 1.2-1.5 Å[7]. As the ionic diameter of lithium cation is 1.20 Å[5], it appeared that 14-crown-4 would be the optimum complexing agent for lithium cation in the crown family[132]. No details could be obtained of the reported synthesis of the positional isomer of 14-crown-4, 1,3,8,10-tetraoxacyclotetradecane[129]. As no synthesis of unsubstituted 14-crown-4 had been published, a research objective was thus to attempt development of a synthesis of 14-crown-4 that would encompass

the desired characteristics stated above for the 12-crown-4 preparation.

Crown Ether Complexes

Metallic Complexes

Introduction. A variety of crown complexes with metal ions have been reported, both in solution and in the crystalline state. The crystalline complexes were generally quite stable, exhibiting melting points well above those of the parent crown and also varying stoichiometries. The following discussion will outline research accomplished in the area.

Crystalline Crown-Cation Complexes. Pedersen was the first to report isolation of solid crown complexes in his classical publications[5,7]. Three procedures were involved in preparing the complexes: (1) reacting different proportions of crown and salt in methanol at 60°C and cooling to room temperature; (2) mixing a salt-methanol solution and different proportions of a crown-methanol slurry at 60°C and cooling to room temperature; and (3) mixing different proportions of crown and salt in methanol and allowing the solvent to evaporate to near-dryness at room temperature. By elemental analyses, stoichiometric ratios of 1:1, 2:1, ad 3:2 (crown:salt) were obtained. Pedersen postulated that the 2:1 and 3:2 complexes were in a "sandwich" configuration. The cation selectivity of dibenzo-18-crown-6 and the developed methanol crystallization procedures

were used to almost quantitatively separate cesium and potassium ions from a common solution[7].

A tremendous variety of crystalline crown-salt complexes have been formed since Pedersen's work and many of the single crystal X-ray studies performed[3-11,17,117,122-123,138-161]. The vast majority of the studies were concerned with alkali and alkali-earth metal cations and substituted crown ethers[17,138-141,146-160]. Su and Weiher observed complex formation between dicyclohexyl-18-crown-6 and a number of transitional metal cations, including Ti(III), V(III), Fe(III), Co(II), and Zn(II)[144]. The crystalline complex derived from $CoCl_2$ was described in detail. Birkbeck, Grace, and Shepherd also formed crystalline complexes from dibenzo-18-crown-6 and several Co(II) salts[145]. Only recently have crystalline complexes of rare-earth metals and crowns have reported[142-143]. Unsubstituted 18-crown-6 was found to form solid 1:1 complexes with potassium tosylate, potassium thiocyanate, and sodium thiocyanate[161-162]. Unsubstituted 16-crown-4 complexed LiBr and LiI in a 1:1 stoichiometry and LiSCN in a 2:1 ratio (crown:salt)[128]. Preparation of 2 solid salt complexes of 12-crown-4 have been reported thus far, including a 1:1 lithium ion complex[122] and a 2:1 pentahydrate complex with sodium chloride[117]. In addition to single crystal X-ray studies of crown complexes, structures of crystalline, uncomplexed 18-crown-6[162] and 1,3,8,10-tetraoxacyclotetradecane[130] have been elucidated. As an

example of the utility of the unambiguous X-ray structure determinations, Bright and Truter demonstrated that 1 of Pedersen's proposed "club sandwich" complexes (3:2 dibenzo-18-crown-6-Rb complex) actually had a unit cell consisting of 2 uncomplexed crown molecules and 4 molecules of 1:1 complex[146,160].

Crown-Cation Complexes in Solution. In addition to crystalline solids, crown ether-cation complexes have also been studied in solution. The formation, stabilities, and stoichiometries of the complexes were determined by far ir spectra[163], uv-visible spectra[163-181] (mainly those studies evaluating ion-pair structures of fluorenyl salts with crown ethers in comparison to earlier studies[173-181] without crown), ^{1}H-nmr[180-181], ^{23}Na-nmr[182-184] and ^{13}C-nmr[185] spectra, esr spectra[186-187], calorimetry[188-192], dielectric permittivity measurements[193], conductance measurements[84,194-195], and polarography[196-200]. A solid electrolyte device based on the dicyclohexyl-18-crown-6-potassium thiocyanate complex has been produced[201]. Using a modification of Pedersen's separation technique[7], Rais and Selucky selectively extracted cesium cation into nonpolar solvents with dibenzo-18-crown-6[202-204]. An excellent review of the literature on solvated crown-cation complexes has recently been published [205].

Biological Utilization of Crown Complexes. Crown ethers were quickly recognized to have complexing properties resembling those of neutral macrocyclic antibiotics, which

influence transport of metal cations across cell membranes via complexation[3,17]. The crowns have thus served as carrier models for the more complex antibiotics (such as nonactin[206]) in membrane transport studies[207-212]. Recent reviews have summarized the literature concerning biochemical research with crown ethers[213-214].

Non-Metallic Crown Complexes

Compared to the tremendous number of metal cation-crown conplexes that have been synthesized[138-141,146-205], relatively few non-metallic crown complexes have been reported[133-134,215-223]. Cram and coworkers synthesized chiral crown ethers that were utilized to separate enantiomers of ammonium salts[133-134]. Molecular complexes of 18-crown-6 and binaphtho-20-crown-6 with arenediazonium-tetrafluoroborate or benzoyl hexafluorophosphate salts were later reported[215]. A change in the ^{1}H-nmr spectra (to slightly lower chemical shift) of the crowns upon solubilization of the salts led to the conclusion that the linear $-N{=}N^{+}$ or $-C{=}O^{+}$ group was being inserted into the "hole" of the macrocycle[215]. The Cram group also produced chiral crowns that selectively complexed enantiomers of α-amino acids in solution[216-217]. Pedersen synthesized high-melting crystalline complexes of crowns with thiourea, related compounds, and 4-phenylsemicarbazide[218]. Urea failed to give a positive result. The stoichiometries were unpredictable, but urea inclusion complexes appeared to be ruled out by the small stoichiometric ratios obtained

(1:1 to 1:6, crown:thio compound). Izatt, Haymore, and Christensen reported a stable crystalline OH_3^+-crown complex characterized by ir[219], while Carbonnel and Rosso have discovered solution clathrate formation between 6-crown-2 (dioxane) and water[220]. Crown complexes with bromine (crystalline)[221], hydrogen bromide (solution)[222], and hydrogen tribromide (solution)[222] have also been reported. Dibenzo-18-crown-6 has been shown to form 1:1 adducts with phenoxymethylpenicillin and salicylic acid in $CHCl_3$[223]. Until the recent discoveries of Harris and Liotta, who reported a high-melting crystalline complex of 18-crown-6 and acetonitrile[107-109], no crown-nitrile complex had been synthesized.

Purpose of Research

Following the discovery of the 18-crown-6-acetonitrile complex[107-109], interest arose in synthesizing other crown-nitrile complexes. A research objective was thus to explore the area of crown-nitrile complexes and to fully characterize successfully-formed crystalline compounds (including the acetonitrile-crown complex). The results of the research have been submitted for publication[224].

Syntheses and Kinetics with Crown Ethers

Reactions with Crowns

Introduction. During the early development of crown ether chemistry, little attention was given to utilization of the solubilized anion for synthetic purposes. The crown complex solutions held great potential, however, due to

improved solubility of the salts in nonpolar solvents, increased dissociation of ion pairs, and the conversion of contact ion pairs into solvent separated ion pairs[3]. In recent years, several researchers have performed syntheses with solubilized crown salt complexes that revealed amazing results in comparison to similar systems without crown.

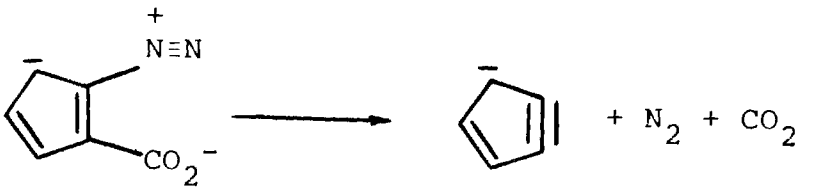
Literature Review. In one of the earliest synthetic utilizations of crown, Fraenkel and Pechhold studied the decomposition of phenylazoformate salts and the alkoxide cleavage of benzoyl-tert-butyl diimide in the presence of dicyclohexyl-18-crown-6[225]. The authors, by dissolving the normally-insoluble substrates in benzene via crown complexation, were able to generate rare organopotassium compounds (phenyl- and tert-butyl potassium) and to study the potent anions.

Staley and Erdman, in studying the decomposition of 6-methyl-6-phenyl-cyclohexadienyl anion (formed from 5-methyl-5-phenyl-1,3-cyclohexadiene with metal amides in liquid NH_3), found that $LiHN_2$ gave a much higher yield of 2-phenyltoluene than did KNH_2[226]. However, upon simple addition of dicyclohexyl-18-crown-6 to the potassium system, the yields nearly equalized. The authors thus concluded that the decomposition route of the anion was greatly influenced by the counterion[226].

Roitman and Cram studied the effect of dicyclohexyl-18-crown-6 on rates and stereochemical course of potassium

alkoxide catalyzed carbanion-generating reactions in alcoholic solvents[227]. In tert-butyl alcohol, cleavage of an optically-active alcohol showed a marked increased inversion of configuration with addition of the crown. The results were attributed to the filling of the coordination sites of the potassium by the crown, thus denying them to the tert-butyl alcohol and resulting in the cation losing its organizing ability at the front face of the carbanion[227].

An interesting study involved attempting to identify dehydrocyclopentadienyl anion, 7, from decomposition of diazacyclopentadiene-2-carboxylate, 6[228]:



6 7

The precursor anion was found to form a complex with dicyclohexyl-18-crown-6 in nonpolar solvents. Using the complex, the authors successfully isolated decomposition products (pyrolysis, neat or in solution) which could have resulted from trapping of 7 with two different trapping agents[227].

Thomassen and coworkers examined the rate of alkylation of potassium phenoxide with butyl bromide in dioxane[228]. They discovered that additions of catalytic dicyclohexyl-18-crown-6 vastly increased the rate of alkylation, that the

reactivity of the phenoxide ion was vastly reduced when linear polyethers were substituted for the crown, and that in a series the rate of reaction reached a maximum when a 6-oxygen crown ring was utilized with the potassium salt.

Staley and Smith found that under normal conditions (33.5% acetonitrile and 66.5% tert-butyl alcohol solvent, 25°C), the reaction of sodium 9-fluorenone oximate with methyl iodide gives a concentration dependent second-order rate constant and oxygen:nitrogen alkylation ratio[229]. Addition of catalytic dibenzo-18-crown-6, however, eliminated the concentration dependence and increased the yield of O-alkylated product. With methyl toxylate, similar effects on the concentration factor was observed on complexation, and totally O-alkylation resulted. The authors attributed their observations to increased effective degree of dissociation of the sodium oximate in the presence of crown[229].

The ability of crown ethers to increase the specific activity of potassium alkoxides in DMSO was investigated by Maskornick[230]. The author, utilizing unsubstituted 18-crown-6, reported that the crown increased dramatically the activity of the salt, apparently satisfying the coordination sites of the cation even to the exclusion of the strongly solvating DMSO[230].

Zaugg and coworkers found that the kinetic and sedimentation properties of alkyl halide-sodio diethyl

n-butylmalonate-binary solvent systems (THF, DME, DMF, or their mixtures with benzene or cyclohexane) showed the reactive species to be a highly solvated ion pair[231]. However, the kinetic behavior with catalytic dicyclohexyl-18-crown-6 appeared to identify the reactive species as a monosolvated ion pair.

Several groups have recently investigated the effects of crown ether addition-elimination reactions. Zavada, Svoboda, and Pankova first found that dicyclohexyl-18-crown-6 leads to a complete reversal of the trans- to cis-olefin ratio (trans-favored with crown) for the elimination of 5-decyl tosylate with potassium tert-butoxide in low-lar solvents[232]. No effect, however, was exerted in dipolar, aprotic solvents. The workers attributed the results to a conversion from contact ion-pairs to solvent-separated ion pairs on crown complexation in solvents of low polarity. Bartsch and coworkers investigated the elimination of 2-bromobutane by various potassium alkoxides in the corresponding alcoholic solvent[233]. Bartsch reported little change in the yield of 1-butene with primary and secondary alkoxides on addition of crown, but a substantial decrease occurred when tertiary alkoxides were used. With all alkoxides, the ratio of trans-2-butene to cis-2-butene significantly increased with crown, apparently independently of the relative percentage of 1-butene. Again, the effect was attributed to increased base dissociation[233]. Naso and coworkers studied the stereochemical course

of elimination from diastereoisomeric 1-deuterio-2-fluoro-2-phenylthioethyl phenyl sulfones[234]. With potassium phenoxide, the anti-stereospecific pathway was increased dramatically at the expense of the syn- course upon addition of dicyclohexyl-18-crown-6. When sodium tert-butoxide was substituted as the base, however, only small changes in the 2 competing pathways were observed. The Naso group also investigated eliminations from halogenoethylenes with fluoride ion in several solvents, including CH_3CN[235]. The formation of acetylenes increased dramatically on addition of dicyclohexyl-18-crown-6 with acetonitrile, but little change occurred in DMF. Butyl cellusolve gave the highest concentration of solubilized fluoride of the 3 solvents with crown, but unsatisfactory yields of acetylene were obtained[235]. Interestingly, no crystalline crown-acetonitrile complex was reported[106-109,224]. A more recent study has shown fluoride ion in 18-crown-6 acetonitrile solution to be a potent base, being especially useful in Michael additions[236]. Borchardt and Saunders found in stereochemical studies of the elimination of 3-hexyltrimethylammonium iodide with potassium tert-butoxide or n-butoxide in their precursor solvents that addition of dicyclohexyl-18-crown-6 surprisingly had no significant effect on the syn-elimination[237]. The lack of crown effect was attributed to the fact that the following equilibrium generates free base, and the macrocycle does not generate

enough additional free base to further increase syn-elimination:

$$RO^-M^+ + RNMe_3^+ + X^- \rightleftharpoons M^+X^- + RNMe_3^+ + RO^-$$

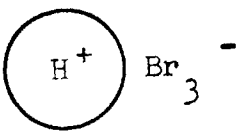
A development of appreciable significance has been the dissolution of alkali metals in organic solvents by addition of crowns. The crown-alkali metal solutions may find application in organic syntheses as reducing agents[3]. Dye, DeBacker, and Nicely formed stable solutions of potassium and cesium metal in THF-dicyclohexyl-18-crown-6 solutions at room temperature, and of potassium with diethyl ether-crown at -78°C[238]. The group later reported that use of dicyclohexyl-18-crown-6 results mainly in the formation of metal anions, while cryptates yielded substantial concentrations of solvated electrons[239]. Kaempf, Lehn, and coworkers extended the latter study to dissolution of the alkali metals in benzene and toluene[33].

Cram, Almy, and Garwood, in a continuation of earlier studies[227], investigated optically pure 3-tert-butyl-1-methylindene-1-H (or -1-D) racemation, isotopic exchange, and isomerization to 1-tert-butyl-3-methylindene in various media[240]. The investigation revealed that addition of catalytic dicyclohexyl-18-crown-6 in a 75% benzene-25% phenol-potassium phenoxide medium sharply reduced the stereospecificities of the isotopic exchange reaction, isomerization reaction, and particularly the exchange rearrangement

reaction. With methanol-O-d-potassium methoxide and in THF-n-propylamine-N-d_2 solvent, crown ether had only a minor effect on the rates of isomerization.

In a useful synthetic application, Sam and Simmons formed a potent oxidant by solubilizing potassium permanganate in benzene by complexation with dicyclohexyl-18-crown-6[241]. Since the example oxidations proceeded cleanly under mild conditions to stoichiometric yields, the reagent was postulated as having analytical as well as synthetic utility.

As a continuation of earlier research[221-222], Schori and Jagur-Grodzinski decided to explore the effect of dicyclohexyl-18-crown-6 on the kinetics of bromination of stilbene in the absence and presence of HBr ($CHCl_3$ solvent)[242]. In the absence of HBr, the crown addition resulted in a small increase in the reaction rate, apparently due to traces of HBr formed in situ. With excess HBr added, the crown acted as a strong inhibitor to the reaction (in contrast to THF). The observations were attributed to a binding of the bromine in a crown-tribromide complex, 8, that was less reactive towards the stilbene (the crown ring represented as a circle):



8

The effect of the addition of dibenzo-18-crown-6 on the decay of the 4H-cyclopenta [def] phenanthrene radical anion has been examined by Timothy and Tabner[243]. The decay of the anion reverted from first-order to second-order kinetics for each of the counterions studied when crown was present. Also, the radical anion was found to be more stable in the presence of crown, especially with sodium and potassium cations.

Matsuda and Koida reported the reduction of ketones with $NaBH_4$ in dibenzo-18-crown-6-aromatic solvent systems[244]. Crown addition increased substantially the yield of alcohol over diglyme and DME addition. Also, the yield of alcohol over the same time period increased with increasing crown concentration.

In an interesting study, Del Cima, Biggi, and Pietra investigated potassium alkoxide substitution of 1-fluoro-2- or 1-fluoro-4-nitrobenzene in the presence of crown[245]. With potassium methoxide-methanol, the crown had little influence on the reaction kinetics, with an ortho:para substitution ratio of 1. A change to potassium-tert-butoxide in tert-butanol, however, revealed that crown addition (equimolar to the nucleophile) increased the rate of reaction of the o-nitrobenzene substrate by 3-fold while that of the p-nitrobenzene substrate increased by nearly 2000. The ortho:para ratio for the tert-butanol reverted from 3.6×10^2 to 1 in the presence of crown.

The Koenigs-Knorr reagents ($AgNO_3$ with alkyl alcohol) have been utilized with dibenzo-18-crown-6 and halide substrates to synthesize glucosides (43-81% yield, room temperature, 1 to 5 minutes)[246]. Methanol gave the highest yield of the solvents studied, while cyclohexanol gave the lowest.

Durst and coworkers have recently published several reports on crown ether catalysis[247-248]. In the first, 90-100% isolated yields of phenacyl esters were produced under mild conditions with catalytic dicyclohexyl-18-crown-6 (potassium acetate and α, p-dibromoacetophenone in refluxing CH_3CN, 15 min)[247]. In the second, the group utilized unsubstituted 18-crown-6 to promote mild, selective reductions of sulfoxides with sodium cyanohydridoborate (mixed solvents of CH_2Cl_2 and alcohol, 58-92% isolated yields)[248]. Several groups have recently investigated generation of carbenes and their subsequent synthetic utilization in syntheses[249-251]. Sepp, Scherer, and Weber reported that diazomethane can be generated with hydrazine hydrate-chloroform-potassium hydroxide-catalytic 18-crown-6 in ether (48% yield)[249]. The yield decreased to 35% on using sodium hydroxide. Makosza and Ludwikow found that many reactions of carbanions and halocarbenes could be effectively catalyzed by dibenzo-18-crown-6, including alkylation of C-H acids, reactions with trichloromethyl anion and dichlorocarbene, reactions of carbanions with aromatic nitro compounds, and Darzens condensations[250]. Phenylhalocarbenes were generated from benzal halides

with potassium tert-butoxide and catalytic 18-crown-6[251]. Omission of 18-crown-6 resulted in α-elimination from the dihalide to give phenylcarbenoids. Dichlorocarbene was generated from $CHCl_3$ and the base with or without 18-crown-6; olefin reactivities were higher for the former case, however.

Sam and Simmons performed displacement and elimination reactions with dicyclohexyl-18-crown-6[252]. Reaction of the potassium iodide complex with 2-bromooctane (in DMF) gave only 2-octene elimination product. Kinetics of the reaction between the potassium bromide or iodide complex with n-butyl brosylate at 25.0°C gave second-order rate constants for primary substitution. Only minor improvement was noted over dissociated tetrabutyl ammonium halide reagents. An unusual nucleophilic aromatic substitution reaction occurred with KOH-crown complex in methanol. Studies showed that anion exchange took place with the solvent to give 89% methoxide anion, and that the generated nucleophile was sufficiently reactive to convert o-dichlorobenzene to a 40-50% yield of o-chloroanisole as the sole product (1.0 M solution of KOH-crown complex in o-dichlorobenzene, 90°C, 16 hr). Reaction under similar conditions with m-dichlorobenzene gave m-chloroanisole in low yields. A benzyne mechanism was eliminated (no m-chloroanisole (with o-dichlorobenzene) or o-chloroanisole (with m-dichlorobenzene) detected) in favor of direct nucleophilic aromatic substitution via a Meisenheimer complex[252].

Following the observation that direct solution of potassium salts can be effected in aprotic organic solvents by 18-crown-6[107], and thereby eliminating the necessity for preliminary complexation[5], Harris, Liotta, and coworkers have utilized the crown to perform a wide variety of substitution, elimination, and addition reactions in acetonitrile and benzene[107,253-254]. The potent nucleophiles, unencumbered by solvation forces, were termed "naked" anions[107,253]. In contradiction to Pedersen's earlier observations with fluorides and substituted crowns[5], unsubstituted 18-crown-6 was shown to be an effective agent for the solubilization of the salt in both solvents, and the anion demonstrated to be both a potent nucleophile and base[253]. Reactions were generally more rapid in CH_3CN than in C_6H_6. In a similar study, "naked" acetate was found to be a weaker base than "naked" flouride, but was also a potent nucleophile[254]. For both anions, reactions were facile and efficient under mild conditions, with near-quantitative yields isolated in many cases.

Nitrile Syntheses without Crown Ethers

Introduction

Organic nitriles have been produced by a variety of preparatory methods[255-444]. In the laboratory, however, displacement and addition reactions by cyanide ion are by far the most widely used methods of synthesizing nitriles. A search of the literature revealed that no investigators had studied the synthetic application of cyanide ion solubilized

in aprotic organic solvents via crown ether complexation. The following sections review the existing literature methods for preparing nitriles[255-444].

Nitriles with Cyanide Ion

One of the earliest and most widely-used preparations of alkyl nitriles involved the displacement of halide ion by cyanide reagents. Although gaseous HCN has been used[255], due to toxicity and reaction simplicity considerations the preferred method was to employ metal cyanides in water, alcohol, or alcohol-water mixtures[255-272]. Early authors used sodium or potassium cyanide in ethanol-water mixtures to prepare primary nitriles[258-265]. Although yields were acceptable on a large scale, the reactions were sluggish, requiring long reaction times and strenuous conditions. For dihalide conversions in the ethanol-water solvent systems, apparently a cyano substituent activates a halogen removed from it by an even number of carbon atoms and inhibits those an odd number of carbons away[255]. For example, 1,3-dichloropropane was much more difficult to convert to the dinitrile[260] than was 1,4-dichlorobutane[255,270]. The tendency toward inhibition diminishes as the chain length increases[255]. Bromide was shown to be displaced by cyanide ion more rapidly than chloride in ethanol-water, e.g., ethylene dibromide was smoothly converted to succinonitrile, but ethylene dichloride was found to be unreactive[255]. Allen utilized the greater reactivity of the bromide to isolate a 40-47% yield of 3-chloro-1-cyanopropane from 3-chloro-1-bromopropane (KCN, reflux,

1-1½ hr)[259]. Sodium and potassium cyanide, in contrast to silver cyanide, was found to give only minor quantitites of isocyanide impurity[255]. As a measure of structure to preferred product in ethanol-water, primary amyl chloride gave a 90% yield of amyl nitrile, secondary amyl chloride produced only a 30% yield (the remainder of the product being olefin), and tertiary amyl chloride gave entirely olefin[271]. With secondary halides, cuprous or silver cyanides were substituted for the alkali metal cyanides with an increase in nitrile yields; the yields were still far below those obtained with primary substrates, however[257,272]. Alicyclic halides generally produce olefins when reacted with cyanide ion, although cyclopentyl bromide has been converted to the nitrile in 27% yield[273]. One comprehensive[255] and several partial[256-257] reviews on nitrile synthesis have appeared.

The preparation of nitriles from alkyl halides in alcoholic solvents was significantly enhanced by utilization of higher-boiling, non-aqueous hydroxy compounds, including ethylene glycol[266-267], liquid poly(ethylene glycols)[268]. and cellusolve[269]. Lewis and Susi exhibited considerable rate increases at primary positions in ethylene glycol over the old ethanol-water systems, and also successfully synthesized secondary (fair yields) and tertiary (poor yields) nitriles by direct displacement in the dialcohol[266]. Kodama and coworkers obtained 1,4-dicyanobutane from 1,4-dichlorobutane, NaCN, and catalytic AcOH smoothly and in high yield in a 50-50 (by weight)

ethylene glycol-tert-butanol solvent mixture[267]. Brandstrom discovered the surprising result that bromides gave moderate yields and slow rates of reaction with cyanide ion in liquid poly(ethylene glycols), while the corresponding chlorides gave excellent yields and fast rates of reaction[268]. As a general rule, bromides are normally displaced more readily than the corresponding chlorides, i.e., the bromide ion is a better leaving group than the chloride. The author postulated that a heterogeneous mechanism was operating, making solubility of the salts involved in the mechanistic sequence an important factor in the relative rates of reaction. A further improvement in the alcohol-cyanide procedure was perfected by Ferguson, who found that utilization of catalytic potassium iodide in cellusolve increased the rate of halide displacement by cyanide ion and also the yield of nitriles over the earlier methods[269].

A significant advancement in nitrile synthesis from alkyl halides was attained with the evolution of dipolar, aprotic solvents and their utilization as reaction media for the cyanide ion displacements, e.g., DMSO and DMF[274-284]. In similar studies, Smiley and Arnold[275] and Friedman and Shechter[276] converted a wide variety of primary and secondary chlorides to the corresponding nitriles with sodium cyanide in DMSO. The conversions occurred rapidly and efficiently to give excellent yields of primary nitriles and much improved (though only fair) yields of the secondary derivatives over

earlier methods. Neopentyl chlorides were converted to nitriles without rearrangement[276]. Chlorocyclohexane gave no substitution product, but a 70% yield of nitrile was obtained with chlorocyclopentane[276]. With potassium cyanide substituted for sodium cyanide, the temperature of the medium had to be maintained above 120°C to effect reaction[275]. The general procedure of these workers has been used synthetically in DMSO, DMF, and other dipolar, aprotic solvents[277-284]. Modifications of the procedure include the substitution of tosylate for halide in the substrate[282] and use of anhydrous lithium cyanide[283] or cyanomethyl copper[284] instead of sodium or potassium cyanide[276]. Kinetic studies performed with methyl iodide and a variety of common nucleophiles in DMF showed that cyanide ion exhibited the highest reactivity toward the substrate[274]. Acetone is a low-boiling, dipolar, aprotic solvent that has been used with some success (especially with catalytic iodide present) in the conversion of halides to nitriles[285].

A more recent development in nitrile synthesis has been phase-transfer catalysis[286-287], whereby catalytic tetraalkylammonium or tetraalkylphosphonium salts are utilized to transfer the cyanide ion across a water-organic interface[288-291]. The yields of nitriles and rates of reaction were generally comparable to those obtained with dipolar, aprotic solvents, while work-up procedures were simpler. An 85-90% yield of displacement product was obtained

with 2-chlorooctane, the highest by any of the reported procedures utilizing direct attack of cyanide ion on a secondary substrate[289]. Although n-octyl methanesulfonate reacted smoothly and effectively with the transferred cyanide, 1-iodooctane and octyl tosylate ceased reacting after 5-30% conversion[289]. A subsequent kinetic investigation with 1-halooctanes revealed several important facts concerning liquid-liquid phase-transfer catalysis (PTC) by quaternary salts: (1) catalysis is directly proportional to the concentration of quaternary salt in the organic phase; (2) the rate is first order in 1-haloalkane concentration; (3) stirring speed is not critical to the rate; (4) the aqueous phase ratio of cyanide ion to chloride ion strongly influences the displacement rate; and (5) the magnitude of the cyanide transfer equilibrium constant depends on a variety of factors, including water volume, relative concentrations of the alkali metal salts, and the polarity of the organic phase[290]. Starks and Owens concluded that reaction was occurring in the organic phase instead of the aqueous phase, at the interface, or in micelles[290]. The 2-phase approach of producing nitriles has recently been applied commercially[291], and several excellent reviews have surveyed the general field of phase-transfer catalysis[286-287].

Several other methods have been introduced that employ cyanide ion for production of nitriles *via* displacement reactions. These include conversion of halides with cyanide

forms of strongly basic anion exchange resins (such as Dowex 21K)[292-293], conversion of aldehydes with hydrazine hydrate-potassium cyanide[294], and conversion of alcohols with sodium cyanide-triphenyl phosphine in DMSO[277].

Displacement of unactivated aromatic halides has been achieved with copper-based cyanides in the substrate as solvent (Rosenmund-von Braun reaction) and in dipolar, aprotic solvents[255,295-298]. An interesting reaction is the von Richter rearrangement, in which halonitrobenzenes give halobenzoic acids on treatment with cyanide ion in aqueous ethanol solvents[299-300]. A more recent study has shown that use of DMSO instead of aqueous alcohol as the reaction solvent gives a complicated mixture of compounds from the potassium cyanide reaction with chloronitrobenzene instead of the usual von Richter product (m-chlorobenzoic acid)[301].

One of the most familiar addition reactions with cyanide ion to produce nitriles is hydrocyanation (addition of HCN across carbon-carbon multiple bonds). Hydrocyanations have been performed (usually on activated olefins) with HCN[302-313], with alkali metal cyanides in water[302], ethanol-water mixutres[302,315], or dipolar, aprotic solvents[316-317], and by cyanide exchange with reactive cyanohydrins[318-321]. With HCN, procedures incorporate the gas alone[302-303] or in conjunction with transition organometallic catalysts (often nickel[307] or palladium[311-313] based). A useful method for

hydrocyanating cyclohexenone derivatives (particularly cholestenone derivatives) that markedly increases the stereoselectivity of the cyanide addition has recently been devised by Nagata and Yoshioka[302,304-306]. The procedure involves the use of HCN and triethylaluminum or performed dialkylaluminum cyanide in an inert solvent. Another hydrocyanation synthesis based on aluminum derivatives and involving conversion of alkynes to unsaturated nitriles has been reported[314]. Additions with cyanide ion in solution are performed in much the same manner as the substitution reactions detailed above, except that a proton donor (e.g., NH_4Cl) is often added to facilitate protonation of the intermediate carbanion[302,315-317]. Improvements over the initial alkali-metal cyanide-ethanol-water systems were use of dipolar, aprotic solvents[316] and tetraalkylammonium cyanide (in a fashion similar to PTC systems)[317]. Cyanohydrins that eliminate HCN readily under mild conditions, such as that of acetone, have been utilized recently to hydrocyanate olefins via cyanide exchange[318-321]. Several reviews on hydrocyanation have been published[255,302,322-323].

The synthesis of 1,4-dicyanobutenes has received special attention due to the commercial importance of the compounds (utilized in Nylon 66 production and in some polyurethane formulations). Methods used to produce either the 1- or 2-butene include direct displacement of the halogens (usually chloride) from 1,4-dihalobutenes by cyanide ion

(HCN or metal cyanides in solution)[324-333], dicyanation of 1,3-butadiene (HCN or CuCN)[333-336], conversion of 1,4-dihydroxybutenes[337], hydrocyanation of 1-cyano-1,3-butadiene[338-340], and recently, dimerization of acrylonitrile (organometallic[341-346] or organophosphorous[347-349] catalysts, styrylphosphine resins[350], or electrolytically[351]). Rearrangement of the 1,4-dicyano-2-butene to the commercially-preferred 1-butene (more readily hydrogenated) has been accomplished by a variety of reagents, including sodium phenoxide[352], piperidine[353], tetraalkylammonium cyanide[317], hydrogenating metals in H_2O or alcohols[354], and CuCl[355]. Crystalline complexes of CuCl and CuBr with both the 1-butene[355] and the 2-butene[356] have been isolated as white powders and their properties analyzed. X-ray studies revealed a 2:1 stoichiometry (salt:butene) regardless of solution temperature on formation. The coordination of all the complexes was pictured as 9:

$$X^-Cu^+ \text{ —— } N\equiv C\text{-}(C_4H_6)\text{-}C\equiv N \text{ —— } Cu^+X^-$$

9

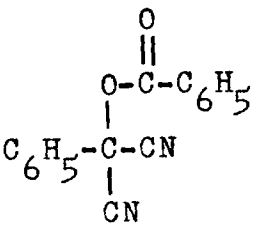
A detailed nmr study of trans-1,4-dicyano-2-butene has been performed[357]. The 1,4-dicyanobutenes are generally converted to adiponitrile by hydrogenation[358-359], and it in turn is hydrogenated to hexamethylene diamine or hydrolyzed to adipic acid (the 2 monomers of Nylon 66). An extensive study of

nitrile formation, with special emphasis on syntheses of 1,4-dicyanobutenes, has been published[360].

Cyanohydrins are also addition products formed by direct attack of cyanide ion. Opening of epoxides gives 2-hydroxynitriles, while attack of ketones or aldehydes (addition of HCN across a carbonyl) gives 1-hydroxynitriles[361]. As the 1-hydroxynitriles are the cyanohydrins of concern in this study, discussion will be limited to these compounds. The cyanohydrins have been produced directly from the ketone with HCN or alkali-metal cyanides, the latter usually in ethanol, ethanol-water, diethyl ether, or acetone as solvent and with a proton donor present (AcOH, NH_4Cl)[361-370]. Several authors have found catalytic KOH to be beneficial to the conversion[371-372]. Others have formed the bisulfite addition product of the ketone or aldehyde before treatment with cyanide ion[373-377]. Novel syntheses of cyanohydrins include use of activated alumina columns with HCN[378] and utilization of exchange reactions between the substrate and commercially-available, reactive cyanohydrins, e.g., acetone cyanohydrin[378-379]. Cyanohydrins are generally unstable, with formation and stability dependent on the steric and strain factors of the ketone[380]. As a result, many authors have studied the equilibria between the ketone, the intermediate alkoxide anion, and the cyanohydrin[381-388]. One report claimed that cyanohydrins could be stabilized against decomposition during distillation by incorporation of 0.001-1.0%

iodine[389]. To avoid unstable, difficult-to-form cyanohydrins as intermediates in the synthesis of α-aminoethyl alcohols from ketones, Evans and coworkers synthesized trimethylsilyl cyanohydrin ethers by trimethylsilyl cyanide addition to the carbonyl[380]. The α-aminoethyl alcohol was then obtained in 1 step with $LiAlH_4$. Several reviews on cyanohydrin syntheses have appeared[361,390-391].

Another interesting utilization of cyanide ion is in addition-elimination reactions. Acyl cyanides have been produced mainly by direct reaction of the acyl chloride with cyanide ion in solution, although indirect methods also exist[392]. For synthesis of benzoyl cyanide, mercuric[393], silver[394-395], and cuprous cyanides[396] have been employed in solution with benzoyl chloride. Gaseous HCN has also been used for direct cyanation of the chloride[397]. Weber and Koenig have recently employed phase-transfer catalysis with NaCN and tetrabutyl ammonium bromide in CH_2Cl_2 to convert benzoyl chloride to the corresponding cyanide in 60% yield[398]. The dimer, α-benzoyloxy-α-phenyl-malononitrile, 10, was formed as a by-product in 35% yield[398]:



10

Although nitriles are not formed as stable products, cyanide ion has also been utilized in dipolar, aprotic solvents to decarbalkoxylate reactive esters such as geminal diesters[399-400] and β-ketoesters[401]. Later studies (including a publication concerning work detailed herein[402]), however, have shown that reactive esters such as diethyl phenylmalonate can be decarbalkoxylated in dry or wet DMSO without added cyanide ion[402-403].

Nitriles without Cyanide Ion

A vast number of syntheses of nitriles, both alkyl and aromatic, have been devised that do not employ cyanide ion directly. As this thesis is concerned only with the direct synthesis of nitriles by cyanide ion substitution, addition, or addition-elimination reactions, only a few examples of each non-direct synthesis will be given. The methods include chemical or thermal transformations of other functional groups to nitriles (ketones[404-405], N-(chlorosulfonyl)amides[406-408], N-(trimethylsilyl)amides[409], amides[410-416], amines[417-418], alcohols[419-420], isothiocyanates[421], aldehydes[422-425], N,N,N-trimethylhydrazonium salts[426], N,N-dialkylhydrazones[427], oximes[428-430], and acids[430-433]), acid-nitrile exchange[434], ammonia oxidation of hydrocarbons[435-436], and displacement of aromatic halides by organometallic cyanides[437] or by assistance of organometallic catalysts[438]. Recent innovative syntheses include photoinduced substitutions of haloaromatics with cyanide ion[439-440], decomposition

of aluminum alkyl chloride-alkyl nitrile complexes[441], pyrolysis of 1,2,5-thiadiazole-1,1-dioxides (dinitrile syntheses)[442], displacement of arylthallium (III) compounds with cyanide[443], and dehydration of amides, thioamides, aldoximes, and ureas with carbenes by phase-transfer catalysis[444].

Purpose of Research

Despite the large number of nitrile syntheses available using cyanide ion, each of the systems present various inadequacies. Reactions in ethanol or ethanol-water mixtures are sluggish and require strenuous conditions and long reaction times. Higher glycols and dipolar, aprotic solvents offer improvements in rate and yields, but require high reaction temperatures and are difficult to separate from the products due to polarity, high boiling points, and solubility in practically all solvents. Liquid-liquid PTC also uses high reaction temperatures, but entails simpler work-up procedures than the earlier methods. A disadvantage of PTC is the high cost or commercial unavailability of the quaternary salts used as catalysts[289]. Due to the improvements over existing syntheses exhibited by H. P. Harris and C. L. Liotta with "naked" fluoride and "naked" acetate[106-107,253-254], and in light of the enhancement of reactivity observed in a variety of other systems with addition of crown ethers[225-252], it was postulated that the 18-crown-6-potassium cyanide complex in aprotic, organic solvents

would present a new, improved synthetic route to nitriles. A research objective was thus to prepare the unsubstituted 18-crown-6-potassium cyanide complex in aprotic, organic solvents (acetonitrile and benzene), and to assess the reactivity of the "naked" cyanide in substitution reactions (primary (mono- and difunctional), secondary (including acyclic rings), tertiary, allylic, benzylic, and aromatic (activated and unactivated) halide substrates), addition reactions (hydrocyanations and cyanohydrin formations), and addition-elimination reactions (attack of acyl chlorides and decarbalkoxylation of reactive esters). Also, a rate study was planned to determine if attack of the "naked" cyanide at primary centers proceeds by bimolecular nucleophilic substitution (Sn2) and, if so, to determine the magnitude of the second-order rate constant for the substrate involved. Most of the synthetic results with "naked" cyanide have recently been published by this author, C. L. Liotta, and C. W. Bowers[445].

CHAPTER VII

EXPERIMENTAL, CROWN ETHERS

Instrumentation

Visual melting points of the 18-crown-6 - nitrile complexes (contained in sealed capillary tubes) were determined on a Mel-Temp device. All reported boiling points and melting points were uncorrected. Conventional infrared (ir) spectra were obtained with a Perkin-Elmer Model 237B Spectrophotometer (neat film (liquids) or nujol mull (solids)), and high-resolution ir spectra with a Perkin-Elmer Model 621 Spectrophotometer (nujol mull). The 1601.4 cm^{-1} absorption of polystyrene was used as a reference peak in all of the ir spectra (positional accuracy of $\pm$ 0.2 cm^{-1} for the high resolution ir). Proton nuclear magnetic resonance (nmr) spectra were secured with either a Varian Model A-60 or T60-A spectrometer utilizing external (12% $CHCl_3$ solution) or internal tetramethylsilane (TMS) as a standard. A JEOL PFT-100 Fourier Transform Spectrometer (TMS internal standard) was employed to obtain proton-decoupled ^{13}C-nmr spectra by signal averaging. Mass spectra were obtained with a Varian M66 mass spectrometer. All elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Georgia. Gas-liquid and preparatory chromatography (glc and glpc) were conducted on a Varian Model 90P chromatograph with a thermal conductivity

detector and using helium carrier gas. For the syntheses monitored by glc, the half-life of reaction ($t_{\frac{1}{2}}$) was defined as the time required for the glc peak area of the starting material to decrease to 50% of the initial value. The time of completion, $t_{completion}$, was defined as the time required for all glc peaks due to starting material and intermediates (where formed) to disappear from the chromatogram. The retention times (t_{ret}) for the glc peaks were determined by first measuring the distance from the beginning of the air peak at the baseline to the beginning of the peak in question in inches. Next, using the known chart speed (0.5 in equaled 1.0 min in all cases), in conjunction with the measured distance, the t_{ret} was calculated. Differential thermal analyses (DTA) and thermogravimetric analyses (TGA) of 18-crown-6 and its nitrile complexes were performed on a Mettler Thermoanalyzer II instrument equipped to plot simultaneous DTA/TGA curves. Constant instrument settings for the DTA/TGA experiments were a TG sensitivity of 100 mg/in, a gas flow rate of 6 lb/hr, a DTA sensitivity of 50 μV/in, a heating rate of 4°C/min, a temperature recording of 2 mv (10 mv full scale), and a chart speed of 12 in/hr. The constant-temperature bath utilized in the kinetic studies was contained in a thick-walled Pyrex glass vessel equipped with a Sargent Thermonitor unit (Model NSI-12) and a calibrated thermometer for temperature control and monitoring. The slopes of the second-order plots were determined by

using the linear regression program of the Wang 700 A/B Advanced Programming Calculator-Computer. The program was arranged to plot the most accurate straight line for data points of the type [x, y] with fixed zero intercept, and to determine the slope of that line.

Chemicals

All extraction solvents and nmr solvents were employed without further purification. Tetrahydrofuran (Fisher, wet), dimethyl sulfoxide (Aldrich), and acetonitrile (Fisher and Aldrich), all reaction solvents, were used as obtained from the manufacturer. Benzene (Fisher) was used directly from the commercial container as a reaction solvent, but was distilled after drying over sodium (bp 80.1°C at 760 mm) for use in the crown-nitrile complex work. Potassium cyanide (Fisher) and potassium chloride (Fisher) were dried in a vacuum desiccator (1 mm, 100°C, 12-15 hr), the flask tightly sealed, and the salts protected against moisture uptake until needed. The other salts employed in the study were utilized without additional treatment.

With the following exceptions, all of the substrates used in the syntheses, complex formations, and kinetic studies were employed without further purification. The substrates 18-crown-6, 1,3-dicyanopropane, and ehtyl-2,4-dicyanopentanoate were synthesized by the author (procedures detailed herein). Practical acrylonitrile (Eastman) was purified after Fieser and Fieser[446]. Commercial glutaronitrile (K & K Lab.) was

dried over $CaCl_2$ and distilled under vacuum (106°C at 0.6 mm). Malononitrile (practical, Eastman) was distilled by T. R. Henson before complexation with 18-crown-6 (bp 109°C at 20 mm).

Safety Considerations

All of the procedures detailed in this chapter present various hazards that require utmost caution and observance of safety procedures in order to avoid serious injury and possible death. A few comments concerning each of these hazards follow.

Potassium Cyanide

The cyanide ion is one of the most toxic substances in existence. Potassium cyanide can be transferred by ingestion, inhalation of the dust, or via "naked" cyanide solution through the skin. In addition, the solid gradually releases hydrogen cyanide produced by attack of moisture and carbon dioxide in air. Fabre has warned that as little as 0.02 - 0.04 mg/liter of hydrogen cyanide in air can prove fatal to humans[447]. Cyanide deaths result through inhibition of the enzyme cytochrome oxidase (by asphyxiation). Mowry has reported that repeated sublethal exposures of cyanide can cause leasions of the central nervous system that can lead to problems in speech, paralysis, anemia, vertigo, and heart and larynx trouble[255].

If a person succumbs to cyanide poisoning, he should be moved to a "clean" area with fresh air, contaminated

clothing removed, and the body covered. While awaiting a physician, Chen, Rose, and Clowes have recommended inhalation of amyl nitrite as a preliminary adjuvant, alternate intravenous injections of sodium nitrite and sodium thiosulfate solutions, and artificial respiration (if necessary)[448]. If possible, pure oxygen inhalation is an added treatment while the medication is being administered[255]. Mowry thus recommends that pearls of amyl nitrite and ampoules of sterile solutions of sodium nitrite and sodium thiosulfate, along with the necessary equipment for injections, be kept in the laboratory in which the cyanide reactions are being conducted[255]. It follows that laboratory personnel should be trained in the proper treatment techniques for cyanide poisoning before an accident occurs.

Nitriles

The mechanisms and symptoms of poisoning by certain nitriles are similar to those of hydrogen cyanide[255]. Although all nitriles are toxic to varying extents, acetonitrile and acrylonitrile are by far the most poisonous ones used or produced in this study.

Lethal amounts of CH_3CN may cause little forewarning discomfort, and the compound may produce severe delayed reactions. A recent publication reported a fatal inhalation exposure to CH_3CN that occurred when the solvent was flushed down an open drain using hot water (bp of CH_3CN, 81.6°C at 760 mm)[449]. Nausea occurred after 4 hr, semiconsciousness

at 12 hr, and death after 6 days. Although antidotes were used, both HCN and CH_3CN were found in all body tissue tested.

Acrylonitrile can cause extensive and painful dermititis when any form of the compound contacts the skin, and emits cyanides when heated or acidified. Although a maximum concentration of 20 ppm has been recommended for acrylonitrile exposure[450], Orusev and Popovski recently reported that workers exposed to the chemical over long periods of time (3-20 mg/m^3 concentration) exhibited abnormal irritativeness, alcohol intolerance, headaches, neurasthenic syndrome, and other ailments[451]. Intravenous intake of 0.085 g/kg was sufficient acrylonitrile to kill a rabbit in 1 test study[452].

Crown Ethers

In his classical publications on crown ether syntheses[4-6], Pedersen reported that the approximate lethal dose of dicyclohexyl-18-crown-6 (closely related in properties to 18-crown-6) was 300 mg/kg for rats (11 min). A dose level of 60 mg/kg/day resulted in no cumulative oral toxicit-. The crown (administered as a 10% propylene glycol solution) caused some generalized corneal injury, iritic injury, and conjunctivitis when placed on the eye. Skin absorption was rapid, with fatality of test animals occurring at 130 mg/kg. Through skin tests, the chemical was classified as an extreme irritant.

Leong and coworkers recently published results of biological tests performed with 12-crown-4[116]. Inhalation exposure

(0.5 or 1.00 ppm, 7 hr/day, 5 days/week) for 3 weeks resulted in marked atrophy of the testicles, prostate gland, and seminal vesicles. In post-exposure studies, testicular atrophy remained for 4 months, while the accessory organs returned to normal appearance and size in 2-3 weeks. Rats subjected to the 12-crown-4 exhibited normal sexual activity, but were sterile. In addition, the exposed animals showed reversible degeneration of conditioned behavioral performance, reductions in food and water intake, growth retardation, and body tremors (attributed to possible affects on the central nervous system).

Other Chemicals

In addition to the nitriles and crown ethers contained in this study, several other utilized chemicals are also especially dangerous. Cyanohydrins are extremely toxic due to their facile elimination of HCN under mild conditions. Both nitrochlorobenzenes (cumulative poison) and dinitrochlorobenzenes are highly toxic, entering the body *via* dust inhalation, ingestion, or skin absorption.

Final Comments

As seen from the data, all of the experimental procedures detailed in this chapter are exceptionally dangerous to perform. Adequate ventilation (properly-functioning hood), careful manipulative techniques (with high-quality rubber gloves, protective goggles, and lab jacket), scrupulous cleanliness of work areas, and good judgment are imperative for repeating these procedures. The safety considerations

especially apply to the "naked" cyanide syntheses. Failure to follow these guidelines may result in permanent physical damage, skin or eye irritation, prolonged sterility, or death.

Syntheses of Crown Ethers

1,4,7,10,13,16-Hexaoxacyclooctadecane (18-Crown-6)

As the author made only a minor contribution to development of the procedure for preparation of 18-crown-6, with the vast majority of the work accomplished by Dr. G. W. Gokel (synthesis) and Dr. H. P. Harris (purification)[105-109], the method is repeated here strictly for completeness. A 5-liter, 3-neck round bottom flask was fitted with a mechanical stirrer (with condenser sleeve), a condenser, and a glass-ground stopper. Into the flask was placed 222.5 g (1.48 mole) of triethylene glycol (Matheson) and 1 liter of commercial tetrahydrofuran (THF, Fisher, wet). A solution of 218.0 g (3.30 mole pure) of 85% potassium hydroxide pellets (Fisher) in 120 ml of water was added to the flask with stirring, and the system stirred for 30 min at ambient temperature. The solution turned a dark brown, and considerable heat was evolved. The stopper was replaced with a 500-ml constant-pressure dropping funnel containing 279.6 g (1.49 mole) of 3,6-dioxa-1,8-dichlorooctane (triethylene glycol chloride, Eastman) in 200 ml of THF, and the chloride solution added to the reaction flask in a thin stream with stirring. The mixture was refluxed for 17 hr, the THF removed by rotary evaporation (aspirator pressure), and the rotary evaporator bath temperature raised

to ca. 70°C to remove the bulk of the water present. One liter of methylene chloride was added to the dark, brown, solid-liquid remains, the mixture stirred, and the salts filtered (aspirator suction) and washed with copius solvent. The methylene chloride solution was dried (anhydrous Mg SO_4, 18 hr), the salt filtered and washed with copious solvent, and the CH_2Cl_2 removed by rotary evaporation (aspirator pressure). Distillation was accomplished by use of a Claisen distilling head with built-in cold finger, thermometer well, and vigreux column. A low-boiling forerun (25-124°C (0.25 mm)) was carefully removed by using low heat, a receiver and pump trap cooled in dry ice-acetone baths, and ice water through the distillation head cold finger. After insuring that the cold trap was not plugged, continued distillation gave 2 fractions boiling over a wide range: 1) a main fraction of relatively pure crown that crystallized on sitting (125-140°C (0.2 mm)); and 2) a dark-colored, solid-liquid slush that also consisted of relatively pure product (140-155°C (0.2 mm)). A total of 159.7 g (41%) of crude 18-crown-6 was obtained.

Each of the 2 fractions was purified separately. The material was placed in an erlenmeyer flask with a Teflon-coated stirring bar and enough acetonitrile to cover the solid (both fractions formed the crown-acetonitrile complex[106-109,224] on contact with the acetonitrile). The mixture was then slowly heated (hood) with stirring until the reflux temperature was

reached. Additional acetonitrile was added to the flask as needed until all of the solid had dissolved. The solution was cooled to room temperature with vigorous stirring to precipitate the white, crystalline crown-acetonitrile complex. The erlenmeyer was capped with a rubber stopper, placed in an ice-acetone bath, and stirring continued to precipitate as much complex as possible. The hygroscopic complex was filtered (aspirator suction) and transferred to a sealed container as quickly as feasible, and the filtrate collected in a 1-liter round bottom flask. The complex from the colored fraction was recrystallized several times in order to attain pure white solid. The acetonitrile was removed (rotary evaporation) from the combined filtrates, and the remains purified by the complex recrystallization procedure using smaller volumes of acetonitrile. All of the white, purified complex obtained was then combined in a 500-ml round bottom flask fitted with a Teflon-coated stirring bar and vacuum take-off. A vacuum hose leading through a pump cold trap (cooled by a dry ice-acetone bath) was attached, and low heat (40-50^{o}C) and pressure (0.1 mm) applied to remove the volatile acetonitrile. As the solid gradually reverted to a slurry after 2-3 hr, stirring resulted in splattering of the complex on the upper portions of the flask. A hot-air gun was used to periodically melt the splattered complex and thus facilitate the complete removal of the solvent. After approximately 12 hr, a viscous oil remained which solidified on sitting to hygroscopic, spherulytic crystals of 18-crown-6 (94.4 g (59% based

on crude product, 24% based on triethylene glycol)): mp 36.5-38°C (lit.[14] mp 39-40°C); nmr peak (CCl_4, internal TMS) at 3.54 (sharp s, $O\underline{CH_2CH_2}O$ of crown) ppm; ir absorptions at 2875 (C-H), 1450 (CH_2), and 1120 (C-O) cm^{-1}; mass spectral peaks at m/e 265 (parent ion), and major fragments at m/e 89, 87, 59, 45, and 44; and ^{13}C-nmr peak ($CDCl_3$, internal TMS, proton decoupled) at 70.742 ppm.

Several repetitions of the procedure were attempted with recovered THF that had been redistilled with a long Vigreux column. Each time, however, addition of the KOH solution resulted in an extremely exothermic reaction, with the system rapidly getting out of control and requiring ice water to prevent a possible explosion. The solution turned a dark black and appeared very viscous. Continuation of the reaction sequence resulted in low yields of 18-crown-6. No such difficulties were encountered while using commercial-grade THF.

1,4,7,10-Tetraoxacyclodocecane (12-Crown-4)

A 250-ml, 3-neck, round bottom flask equipped with an internal thermometer, reflux condenser, glass-ground stopper, and magnetic stirring bar was charged with 70 ml of dimethyl sulfoxide (DMSO, Aldrich) and 9.3 g (0.23 mole) of sodium hydroxide (98% pellets, Fisher). After stirring for 5 min, 24.6 g (0.23 mole) of anhydrous lithium perchlorate (City Chem. Corp.) was added in 1 portion. During stirring (10 min), the mixture attained a milky appearance and warmed to approximately 60°C. A solution of 6.26 g (0.10 mole) of

ethylene glycol (Fisher) in 15 ml of DMSO was poured into the flask in 1 portion, and the resulting mixture stirred for 15 min. The stopper was replaced with a 60-ml constant-pressure dropping funnel containing a solution of 18.7 g (0.10 mole) of 3,6-dioxa-1,8-dichlorooctane (triethylene glycol chloride, Eastman) in 15 ml of DMSO, and the liquid added to the reaction flask in a thin stream with vigorous stirring. The solution was heated at 100-110°C for 22 hr, the salts filtered and washed with copious amounts of chloroform, the filtrate added to 500 ml of distilled water, and the aqueous solution extracted with 4-200 ml aliquots of chloroform. The combined extracts were dried (anhydrous $MgSO_4$, 3 hr), the salt filtered and washed with copious amounts of chloroform, and the solvent removed by rotary evaporation (aspirator pressure). Distillation of the remains gave 2.5 g (14%) of hygroscopic 12-crown-4 as a colorless liquid: bp 67-70°C at 0.5 mm (lit.[113] bp 118-119°C (15 mm)); ^{1}H-nmr peak ($CDCl_3$, external TMS) at 3.65 (sharp s, $OC\underline{H}_2C\underline{H}_2O$ of crown) ppm; ^{13}C-nmr peak ($CDCl_3$, internal TMS, proton decoupled) at 70.621 ppm; ir absorptions (neat, NaCl plates) at 2925 (C-H), 1465 (CH_2), 1280 and 1250 (cyclic ether), 1130, 1100, and 1095 (C-O), and 920 (cyclic ether) cm^{-1}; and mass spectra peaks with relative abundances at m/e 176 (parent ion, magnified), 133 (30%), 89 (94%), 87 (56%), 73 (70%), 59 (57%), and 45 (100%). A trace of DMSO in the final product (as evidenced by a weak nmr

singlet at 2.65 ppm) was removed by careful redistillation, and residual water (as evidenced by ir absorption bands at 3250 (broad, O-H) and 1625 (sharp, H_2O) cm^{-1}) in the hygroscopic 12-crown-4 was greatly reduced by allowing the crown to stir over molecular sieve adsorbent under nitrogen for 12 hr. The ^1H-nmr, ^{13}C-nmr, and ir spectra corresponded to those reported in the literature for 12-crown-4 synthesized by acid-catalyzed cyclic tetramerization of ethylene oxide[120]. The ir spectra was also similar to that recorded for 1,4-dioxane[453].

Elemental analysis for $C_8H_{16}O_4$:

Calculated: C, 54.53; H, 9.15.

Found: C, 54.31; H, 9.15.

Attempted Preparation of 1,4,8,11-Tetraoxacyclotetradecane (14-Crown-4).

The apparatus was the same as in the synthesis of 12-crown-4. Into the reaction flask was placed 70 ml of DMSO (Aldrich) and 16.8 g (0.42 mole) of sodium hydroxide (98% pellets, Fisher). After stirring for 5 min, 44.7 g (0.42 mole) of anhydrous lithium perchlorate (City Chem. Corp.) was added in 1 portion, heat was evolved, and the cloudy mixture was stirred for 10 min. A solution of 12.41 g (0.20 mole) of ethylene glycol (Fisher) in 30 ml of DMSO was added in 1 portion, and the mixture stirred for 15 min while raising the flask temperature to 110°C. A solution of 22.60 g (0.20 mole) of 1,3-dichloropropane (Aldrich) in 30 ml of DMSO was added

in a thin stream from a dropping funnel, the mixture held at 110°C with vigorous stirring for 22 hr, and the solution worked-up as in the synthesis of 12-crown-4. Distillation gave 1 fraction (0.25 g) in the expected boiling range of 14-crown-4 (83-85°C at 0.5 mm, extrapolated from the bp of 12-crown-4 (67-70°C at 0.5 mm)). Nmr analysis (C_6H_6, external TMS) showed the fraction to be impure, but 3 major bands that were conceivably due to 14-crown-4 were the prominent features of the spectra: 3.30 (8H, sharp s, $OC\underline{H}_2C\underline{H}_2O$), 3.05 (8H, "spiked" band (3 peaks), $OC\underline{H}_2CH_2C\underline{H}_2O$), and 1.40 (4H, broad m with 5-6 overlapping peaks, $OCH_2C\underline{H}_2$-CH_2O) ppm. Due to the impurities present and the low yield of suspected 14-crown-4 obtained (0.25 g crude (0.6%)), no attempt was made to further purify and analyze the isolated material.

Complexes of 18-Crown-6 with Nitrile Compounds

Syntheses of Crown-Nitrile Complexes

The hot, saturated solutions for preparation of the acetonitrile-, acrylonitrile-, glutaronitrile-, adiponitrile-, and δ-chlorovaleronitrle-crown complexes were formed by first adding sufficient 18-crown-6 to 5 ml of the neat nitrile compound in a 10 ml erlenmeyer flask to saturate the solution (at 25°C), and then adding further amounts of crown with gentle heating (hot-air gun) until solubilization became difficult. The hot solution was allowed to slowly cool to room temperature, at which point the crown-nitrile complex

precipitated spontaneously or a supersaturated solution was formed. In the latter case, crystallization was induced by seeding (the seeds prepared by forming a small amount of supersaturated (at 25°C) solution in a test tube, and initiating crystallization at low temperatures) and/or further cooling in an ice-acetone bath. The hygroscopic crystals were isolated in all cases by filtration in a glove box under nitrogen, utilizing a Buchner funnel and aspirator suction to insure the complete separation of uncomplexed liquid from the solid. The solubility of the crown in acetonitrile was found to be ca. 0.2 M at room temperature[106]. Even at this low concentration, however, the acetonitrile-crown complex precitates after sitting undisturbed for long periods[106-109,224]. In each of the following preparations, molecular ratios listed are in the order of molecules of 18-crown-6 to molecules of nitrile compound, e.g., a 1:2 complex of acetonitrile and crown indicates a stoichiometry of one molecule of crown and two molecules of acetonitrile. The relative hydrogens by nmr integration are approximate, with the exact, normalized ratios contained in Table 6. The succinonitrile- and malononitrile-crown complexes were synthesized, partially characterized, and supplied by T. R. Henson[236].

Preparation of Acetonitrile-Crown Complexes. A small Teflon-coated magnetic bar was added to the hot, saturated solution of 18-crown-6 in acetonitrile, and the liquid cooled slowly with vigorous stirring to room temperature. Fine,

white crystals of crown-acetonitrile complex precipitated spontaneously and were isolated: mp 63.5-65.5°C (mp of pure 18-crown-6, 36.5-38°C); ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 2.00 (9H, sharp s, $C\underline{H}_3CN$) and 3.60 (48H, sharp s, crown) ppm; ir absorption (high resolution, nujol mull) at 2234 (C≡N) cm^{-1}.

Elemental analysis:

Calculated (1:2 complex): C, 55.47; H, 8.73; N, 8.09

Found: C, 55.44; H, 8.72; N, 7.98

The complex was recrystallized from carbon tetrachloride by warming an excess amount of the solid in the chlorinated solvent until solubilization was achieved, cooling the solution to room temperature to precipitate the fine white crystals, and isolating the solid: mp 62.5-65.5°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 2.00 (9H, sharp s) and 3.52 (48H, s) ppm.

In a modification of the procedure, the hot, saturated solution of crown in acetonitrile was allowed to cool slowly to room temperature without disturbance. Stacked, transparent platelets of complex were isolated after several days: mp 72-75°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 2.00 (6H, s, $C\underline{H}_3CN$) and 3.55 (24H, s, crown) ppm; and ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) at 117.158 ($CH_3\underline{C}N$) and 70.681 (crown) ppm.

Elemental analysis:

Calculated (1:2 complex): C, 55.47; H, 8.73; N, 8.09

Found: C, 55.37; H, 8.78; N, 7.98

The platelets were recrystallized in CCl_4 to give fine crystals of acetonitrile complex: mp 70-72°C; and nmr peaks (CH_2Cl_2, external TMS) at 1.95 (6H, s) and 3.55 (24H, s) ppm.

Preparation of Acrylonitrile-Crown Complex. The hot, saturated solution of 18-crown-6 in acrylonitrile was cooled to room temperature, and a small seed added to initiate single crystal growth. The isolated cubic platelets exhibited the following properties: mp 34.5-35.5°C; ^{1}H-nmr peaks (CCl_4, external TMS) at 3.55 (48H, s, crown), and 6.00 (9H, complicated m, $C\underline{H}_2{=}C\underline{H}(CN)$) ppm; ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) at 116.915 ($CH_2{=}CH(\underline{C}N)$) and 70.681 (crown) ppm; and ir absorption (high resolution, nujol mull)) at 2207 ($C{\equiv}N$) cm^{-1}.

Elemental analysis:

Calculated (2:3 complex): C, 57.62; H, 8.35; N, 6.11

Found: C, 57.52; H, 8.34; N, 6.16

Attempts to recrystallize the platelets from CCl_4, hexane, and mixtures of the 2 failed.

Preparation of Glutaronitrile-Crown Complex. Crystallization of the supersaturated (at 25°C) solution of 18-crown-6 in glutaronitrile was initiated by seeding, and the fine needle crystals of glutaronitrile-crown complex isolated: mp 47-48°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 2.10 (4H, m, $CH_2(CN)C\underline{H}_2CH_2(CN)$), 2.55 (8H, t, $C\underline{H}_2(CN)CH_2$), and 3.60 (24H, s, crown) ppm; and ir absorption (high resolution,

nujol mull) at 2231 (C≡N) cm^{-1}. The complex was recrystallized from CCl_4 to give uniform needle crystals of the complex; mp 47.5-49°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 2.08 (4H, m), 2.52 (t, 8H), and 3.60 (24H, s) ppm; and ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) at 118.308 ($CH_2CH_2(\underline{C}N)$) and 70.560 (crown) ppm.

Elemental analysis:

Calculated (1:2 complex): C, 58.38; H, 8.02; N, 12.38

Found: C, 58.26; H, 8.05; N, 12.30

Preparation of Adiponitrile-Crown Complex. The fine needle crystals were prepared from adiponitrile and 18-crown-6 by seeding the supersaturated (at 25°C) solution and isolating the complex: mp 50-52°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 1.80 (12H, m, $CH_2(CN)C\underline{H}_2C\underline{H}_2$), 2.45 (12H, t, $C\underline{H}_2(CN)CH_2$) and 3.60 (24H, s, crown) ppm. The complex was recrystallized from CCl_4 to give long, uniform needle crystals of adiponitrile-crown complex: mp 51-52°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 1.80 (12H, m), 2.45 (12H, t), and 3.60 (48H, s) ppm; ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) at 119.100 ($CH_2(\underline{C}N)$) and 70.560 (crown) ppm; and ir absorption (high resolution, nujol mull) at 2227 (C≡N) cm^{-1}. The original complex was also recrystallized from C_6H_6 and the solid dried under vacuum desiccation (1.0 mm, 25°C) to give long, uniform needle crystals: mp 51-52°C; ^{1}H-nmr peaks ($CDCl_3$, external TMS) at 1.90 (m), 2.50 (m), and 3.75 (s) ppm (uncertain stoichiometry).

Elemental analysis (C_6H_6-recrystallized complex):

Calculated (1:1 complex): C, 58.04; H, 8.66; N, 7.52

Calculated (2:3 complex): C, 59.13; H, 8.51; N, 9.85

Found: C, 61.35; H, 8.73; N, 7.18

Preparation of δ-Chlorovaleronitrile-Crown Complex. The hot, saturated solution of 18-crown-6 in δ-chlorovaleronitrile was cooled to 25°C and seeded to precipitate fine needle crystals of the complex: mp 36.5-38°C; ^{1}H-nmr peaks (CH_2Cl_2, external TMS) at 1.82 (4H, m, internal $C\underline{H}_2$), 2.40 (2H, t, $CH_2C\underline{H}_2(CN)$), 3.57 (2H, t (masked by crown singlet), $CH_2C\underline{H}_2(Cl)$), adn 3.60 (24H, s, crown) ppm.

Elemental analysis:

Calculated (1:1 complex): C, 53.46; H, 8.45; N, 3.67

Found: C, 53.21; H, 8.20; N, 4.18

Preparation of 1,2-Dicyanopropane-Crown Complex. The crystalline complex was isolated from the condensed solution of 1,2-dicyanopropane and 18-crown-6 (see the hydrocyanation reaction, preparation of 1,2-dicyanopropane). The solid consisted of fine, light tan particles: mp 69-70.5°C; ^{1}H-nmr peaks ($CHCl_3$, external TMS) at 1.80 (6H, d, $CH(CN)C\underline{H}_3$), 2.90 (4H, d, $C\underline{H}_2(CN)CH(CN)$), 3.20 (2H, m, $CH_2(CN)C\underline{H}(CN)CH_3$), and 3.75 (24H, s, crown) ppm. The solid was recrystallized from CCl_4 to obtain white, fine crystalline particles of 1,2-dicyanopropane-crown complex: mp 70-70.5°C; ^{1}H-nmr peaks ($CHCl_3$, external TMS) at 1.80 (6H, d), 2.90 (4H, d), 3.20 (2H, m), and 3.75 (24H, s) ppm.

Elemental analysis:

Calculated (1:2 complex): C, 58.38; H, 8.02; N, 12.38

Found: C, 58.69; H, 7.89; N, 12.57

Preparation of Succinonitrile-Crown Complex. The complex was synthesized, partially characterized, and supplied by T. R. Henson[236], and thus its preparation is repeated herein only for completeness. Into a 25-ml erlenmeyer flask was placed 8 ml of dry benzene, 0.20 g (0.0025 mole) of succinonitrile, and 1.00 g (0.0038 mole) of 18-crown-6. The flask was heated until the solid dissolved, cooled to room temperature, and placed in an ice water bath. Uniform needle crystals were precipitated, filtered, and dried under vacuum desiccation: mp 83-84°C. The solid was recrystallized from CCl_4 to give long needle crystals: mp 83-84°C; ^{1}H-nmr peaks ($CDCl_3$, internal TMS) at 2.90 (8H, s, $C\underline{H}_2(CN)C\underline{H}_2(CN)$) and 3.70 (24H, s, crown) ppm; ^{13}C-nmr peaks ($CDCl_3$, internal TMS, proton decoupled) at 118.129 ($CH_2(C\underline{N})$) and 70.713 (crown) ppm; and ir absorption (high resolution, nujol mull) at 2221 (C≡N) cm^{-1}.

Elemental analysis:

Calculated (1:2 complex): C, 56.58; H, 7.60; N, 13.20

Found: C, 57.06; H, 7.68; N, 13.28

Preparation of Malononitrile-Crown Complex. The complex was synthesized, partially characterized, and supplied by T. R. Henson[236], and thus the procedure is repeated herein only for completeness. Into a 25-ml erlenmeyer flask were

placed 8 ml of dry benzene, 2.00 g (0.0076 mole) of 18-crown-6, and 1.50 g (0.023 mole) of malononitrile. The solution was heated until the solids dissolved, the flask cooled to room temperature, and the white complex allowed to precipitate undisturbed. The material was filtered, dried under vacuum desiccation (1 mm, 25°C), and recrystallized from dry C_6H_6 to give uniform needle crystals of malononitrile-crown complex: mp 127-129°C; ^{1}H-nmr peaks (CD_3CN, internal TMS) at 3.70 (24H, s, crown), and 3.90 (4H, s, $C\underline{H}_2(CN)_2$) ppm; ^{13}C-nmr peaks (acetone-d_6, internal TMS, proton decoupled) at 113.275 ($CH_2(\underline{C}N)_2$) and 70.742 (crown) ppm; ^{13}C-nmr (CD_3CN, internal TMS, proton decoupled) at 112.790 ($CH_2(\underline{C}N)_2$) and 70.985 (crown) ppm; and ir absorption (high resolution, nujol mull) at 2242 (C≡N) cm^{-1}.

Elemental analysis:

Calculated (1:2 complex): C, 54.53; H, 7.12; N, 14.14

Found: C, 54.47; H, 7.14; N, 14.16

Attempted Preparation of Benzonitrile-Crown Complex.

The supersaturated solution of 18-crown-6 in benzonitrile gave no complex at room temperature. It was observed that the system froze to a transparent glass on cooling in a dry ice-acetone bath, reverted to a crystalline substance on slow warming, and melted before reaching room temperature. The crystals could be formed directly in an ice-acetone bath (-5 to -10°C). Using an internal low-temperature thermometer, it was determined that the crystals (spherulitic) melted in the range -2 to +2°C.

DTA/TGA Analyses of Crown-Nitrile Complexes

Differential thermal analyses/thermogravimetric analyses were performed for a number of the 18-crown-6-nitrile complexes utilizing a Mettler Thermoanalyzer II instrument. Plotted simultaneously were the actual weight loss and weight loss-times-ten curves (TGA), DTA curves, and temperature curves. An air filter containing anhydrous calcium sulfate was placed between a small air pump and the air-intake valve of the instrument in order to supply the system with a steady flow of dry air. Standard conditions employed were sample sizes of 50-105 mg, the use of dry aluminum oxide as a standard, the use of macro-size platinum crucibles, and an atmosphere of dry air. The Thermoanalyzer was set up according to the manufacturer's instructions (see the Instrumentation section for constant settings). The material to be tested was crushed in a dry box and placed in a desiccator until used. The platinum crucibles were removed from the oven, cooled, weighed, and dry aluminum oxide weighed into the crucibles (250-300 mg of the standard in the reference crucible and that amount less the weight of complex used in the sample crucible). The sample was weighed into the sample crucible, mixed well with the aluminum oxide, and the 2 crucibles placed on the proper posts of the ceramic thermocouple unit. The machine was calibrated to the relative weights of the 2 crucibles, the oven placed around the sample, and the air flow regulated to 6 lb/hr. After running the recorder several minutes to

insure equilibration, heating was begun and the graphs plotted automatically over a period of several hours. After shutdown and cooling of the furnace, the crucibles were placed in an oven in preparation for the next run, i.e., the crucibles were heated at 900°C for a minimum of 3 hr in a ceramic furnace between runs to insure complete pyrollization and removal of organic material and to redry the aluminum oxide standard.

The critical data recorded from the graphs were the behavior of the DTA/TGA curves up to and at the melting point of the complex, the weight loss of the sample in the same region, and the recorded mp (accurate to approximately ± 3°C). DTA/TGA of pure 18-crown-6 demonstrated that the compound was thermally degrading above 120°C, and thus the characteristics of the graphs above the melting point were neglected. The DTA curve up to the mp was inspected closely for any exothermic or endothermic peaks occurring, and the TGA curve inspected for significant weight loss in the same region. The graph paper was calibrated in 1 mg units, and thus the weight loss of the complex tested for any given region of the DTA curve was found by directly reading the number of units that the TGA weight curve dropped over the concerned region. The per cent loss was calculated by assigning the initial weight of the complex to the level portion of the TGA curve at 25°C, and dividing that quantity into the weight loss for the concerned DTA region. The solid-liquid phase transition for each complex was exhibited by an

endothermic peak occurring over the mp range. The recorded mp was found by projecting the point of the peak (indicating maximum conductivity difference between the sample and standard crucibles) to the plotted temperature curve, and projecting that point in turn to the temperature scale previously transferred onto the graph paper (origin at 25°C). The behavior of the curves determined whether the material tested was a stable complex, an unstable complex, or a solvate.

The crown-nitrile complexes tested by DTA/TGA experienced no transitions, either endothermic or exothermic, below the melting points. The endothermic mp peak temperature and the per cent weight losses (where applicable) at the mp were as follows for the complexes tested: acetonitrile-crown (fine particles, 60°C (10.5%)); acetonitrile-crown (plate crystals, 68°C (14.4%)); glutaronitrile-crown (50°C); adiponitrile-crown (recrystallized in C_6H_6, 53°C); succinonitrile-crown (recrystallized in CCl_4, 87°C); malononitrile-crown (recrystallized in C_6H_6, 130°C (2.7%)); 1,2-dicyanopropane-crown (recrystallized in CCl_4, 71°C), and δ-chlorovaleronitrile (40°C). For complexes without a listed weight loss, the actual loss up to the mp was negligible (less than 1%). The solids without given recrystallization information were the original complexes isolated. DTA/TGA analysis of the acrylonitrile-crown complex was attempted, but no endotherm was observed in the expected mp region. In the region of the visually-determined mp (34.5-35.5°C), a weight loss

of 3.8% was observed *via* the TGA curve for the acrylonitrile-crown complex.

Reactions Utilizing "Naked" Cyanide

Apparatus

The apparatus for the cyanide reactions was the same in all cases. The reaction pot was a 50-ml, 1- or 3-neck round bottom flask (14/20 standard-tapered joints) equipped with a Teflon-coated stirring bar (1" x 3/8" required, as vigorous stirring facilitated complete reaction[106]), a condenser topped by a drying tube (calcium sulfate or chloride), and (for the 3-neck flask) 2 glass-ground stoppers. Withdrawal of solution aliquots for analyses during the course of reaction was accomplished by halting the stirring bar, quickly inserting an elongated pipette through the condenser into the flask, and withdrawing (suction bulb) the liquid. Stirring was continued as soon as possible to avoid "bumping" in the reflux systems. The withdrawn aliquots were placed in ½-dram vials, centrifuged to compact the salt present, and the liquid carefully pipetted off the solid. The glc syringe utilized (Hamilton, 10 μl, gas-tight) was rinsed thoroughly with water followed by acetone if long periods elapsed between injections in order to free the barrel of salt particles. For short time periods between tests, acetone washings were performed after each injection. After injection was performed, the aliquot was returned to the reaction flask *via* a pipette through the condenser.

Displacement and Elimination Reactions

1-Cyanohexane, Method I. Into a 25-ml volumetric flask were placed 5.43 g (0.045 mole) of 1-chlorohexane (Eastman), and the volume diluted to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 0.93 g (0.0035 mole)) in acetonitrile to give a final solution concentration of 1.8 M in reactant and ca. 0.14 M in crown. Six grams (0.093 mole) of dry, powdered potassium cyanide was placed in the reaction flask, the prepared solution poured directly over the solid, and the system brought to reflux with vigorous stirring. The course of the reaction was monitored by glc analysis (3% SE 30, 5' x ¼", 65°C), which showed a $t_{\frac{1}{2}}$ of 0.2 hr, a $t_{completion}$ of 2.2 hr, and a yield of ca. 100% of 1-cyanohexane. The system was refluxed for an additional 0.8 hr to insure complete conversion, the flask cooled, and the salts filtered (aspirator suction), and washed with acetonitrile. The solution was reduced to ca. 1/3 volume by rotary evaporation (aspirator pressure), the remains extracted with methylene chloride (continuous extraction, 24 hr), and the methylene chloride solution dried (anhydrous magnesium sulfate, 24 hr). The salt was filtered (aspirator suction), and the solvent removed by rotary evaporation (aspirator pressure). Distillation gave 4.53 g (91%) of 1-cyanohexane as a colorless liquid: bp 81-83°C at 25 mm (lit.[454] bp 183°C at 765 mm); nmr peaks (neat, external TMS) at 2.12 (2H, t, $\underline{CH_2}(X)CH_2$), 1.25 (8H, broad, multi-peak m, internal $\underline{CH_2}$), and 0.73 (3H,

t, $CH_2\underline{CH_3}$) ppm; ir absorptions (neat, NaCl plates) at 2930 (C-H), 2245 (C≡N), 1460 (CH_2), and 1380 (CH_3) cm^{-1}; and mass spectral peaks with relative abundances at m/e 111 (parent ion, 1%), 110 (62%), 82 (100%), 55 (49%), 43 (72%), 41 (80%), 29 (31%), and 27 (42%).

1-Cyanohexane, Method II. Into a 25-ml volumetric flask were placed 7.43 g (0.045 mole) of 1-bromohexane (Eastman), and the volume diluted to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 0.93 g (0.0035 mole)) in acetonitrile to give a final solution concentration of 1.8 M in reactant and ca. 0.14 M in crown. A total of 6.31 g (0.098 mole) of dry, powdered potassium cyanide (Fisher) were employed, and the reaction procedure was as in Method I. Glc analysis (3% SE 30, 5' x ¼", 90°C) showed a $t_{½}$ of 10 hr, a $t_{completion}$ of 40 hr, and a yield of ca. 100% of 1-cyanohexane. The glc retention time and nmr analysis of the product in solution was the same as that for the fully characterized sample of 1-cyanohexane isolated in Method I.

Benzyl Cyanide, Method I. Into a 25-ml volumetric flask were placed 6.73 g (0.053 mole) of benzyl chloride (Fisher) and the volume diluted to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 0.93 g (0.0035 mole)) in acetonitrile to give a final solution concentration of 2.1 M in reactant and ca. 0.14 M in crown. The solution was poured over 6.60 g (0.10 mole) of dry, powdered potassium cyanide, the mixture stirred at ambient temperature, and an exothermic

reaction observed (the solution did not reflux). Glc analysis (3% SE 30, 5' x ¼", 120°C) showed a $t_{½}$ of 0.08 hr, a $t_{completion}$ of 0.4 hr, and a yield of ca. 100% of benzyl cyanide. The salts were filtered and washed with acetonitrile, and the solution worked up as in the synthesis of 1-cyanohexane, Method I. Distillation gave 5.87 g (94%) of benzyl cyanide as a colorless liquid: bp 76-78°C at 2.0 mm (lit.[455] bp 85°C at 3 mm); nmr peaks (neat, external TMS) at 7.00 (5H, sharp s, aromatic CH) and 3.15 (2H, sharp s, $C_6H_5CH_2$)X)) ppm; ir absorptions (neat, NaCl plates) at 3070 (aromatic C-H), 3030 (alkane C-H), 2250 (C≡N), 1600 (C=C), 1440 (C=C-H), 1425 (CH_2), and 726 (aromatic C=C) cm^{-1}; and mass spectral peaks with relative abundances at m/e 117 (parent ion, 100%), 90 (54%), 77 (9%), 62 (14%), and 51 (16%). An identical run as above, but without 18-crown-6, gave (by glc analysis) ca. 20% yield of benzyl cyanide after 75 hr at ambient temperature.

Benzyl Cyanide, Method II. Into a 25-ml volumetric flask were placed 7.71 g (0.45 mole) of benzyl bromide (Aldrich) and the volume diluted to the mark with 0.185 M stock solution of 18-crown-6 (ca. 0.98 g (0.0037 mole)) in acetonitrile to give a final solution concentration of 1.8 M in reactant and ca. 0.15 M in crown. The prcedure was the same as in Method I. Glc analysis (3% SE 30, 5' x ¼", 105°C) showed a $t_{½}$ of 13 hr, a $t_{completion}$ of 25 hr, and a yield of ca. 100% of benzyl

cyanide. Nmr integration analysis (CH_3CN, external TMS) of the benzyl bromide reactant solution (7.05 ppm, sharp s, aromatic C<u>H</u>; 4.25 ppm, sharp s, $C_6H_5C\underline{H}_2Br$; and 3.20 ppm, sharp s, $OC\underline{H}_2C\underline{H}_2O$ of 18-crown-6) gave a benzyl methylene:crown ratio of 1.20:1. Similar integration analysis of the benzyl cyanide product solution (7.10 ppm, sharp s, aromatic C<u>H</u>; 3.55 ppm, sharp s, $C_6H_5C\underline{H}_2CN$; 3.30 ppm, sharp s, $OC\underline{H}_2C\underline{H}_2O$ of 18-crown-6) gave a benzyl methylene:crown ratio of 1.21:1 (<u>ca.</u> 100% yield of benzyl cyanide). The glc retention time and nmr analysis of the product in solution were identical to the fully characterized sample of benzyl cyanide isolated in Method I.

<u>1,3-Dicyanopropane, Method I</u>. Into a 25-ml volumetric flask were placed 5.08 g (0.045 mole) of 1,3-dichloropropane (Aldrich), and the volume diluted to the mark with a 0.185 <u>M</u> stock solution of 18-crown-6 (<u>ca.</u> 1.0 g (0.0038 mole)) in acetonitrile to give a final solution concentration of 1.8 <u>M</u> in reactant and <u>ca.</u> 0.15 <u>M</u> in crown. The solution was poured over 11.78 g (0.18 mole) of dry, powdered potassium cyanide, the system brought to reflux with vigorous stirring, and the course of the reaction followed by glc analysis (3% SE 30, 5' x ¼", 65°C). The glc analysis showed a $t_{\frac{1}{2}}$ of 0.2 hr and a $t_{completion}$ of 1.5 hr. The analysis also exhibited a peak intermediate in retention time between the starting material and the product (assumed to be monocyanated intermediate, 1-chloro-3-cyanopropane) that grew to a maximum peak height during the course of the reaction and decreased to the baseline

by $t_{completion}$. The system was refluxed an additional 0.25 hr to insure completion and the reaction mixtured worked-up as in the synthesis of 1-cyanohexane, Method I. Distillation gave 4.10 g (97%) of 1,3-dicyanopropane as a colorless liquid: bp 78-82°C at 0.15 mm (lit.[456] bp 286°C at 760 mm); nmr peaks (neat, external TMS) at 2.48 (4H, t, $C\underline{H}_2(X)CH_2$) and 1.95 (2H, m, $CH_2(X)C\underline{H}_2$); ir absorptions (neat, NaCl plates) at 2950 (CH_2), 2240 ($C\equiv N$), and 1425 (CH_2) cm^{-1}; and mass spectral peaks with relative abundances at m/e 94 (parent ion, magnified), 54 (99%), 41 (100%), 28 (52%), and 27 (30%). The glc, ir, and nmr analyses of the synthesized compound were identical to those of commercial 1,3-dicyanopropane (K & K Lab.).

The reaction was repeated, except that the product solution was placed in 75 ml of distilled water and hand-extracted with 4-50 ml aliquots of methylene chloride. Work-up and distillation gave 3.91 g (92.5%) of 1,3-dicyanopropane.

1,3-Dicyanopropane, Method II. A 25-ml volumetric flask was charged with 9.10 g (0.045 mole) of 1,3-dibromopropane (Eastman) and the solution diluted to the mark with a 01185 M stock solution of 18-crown-6 (ca. 1.0 g (0.0038 mole)) in acetonitrile to give a final solution concentration of 1.8 M in reactant and ca. 0.15 M in crown. The solution was poured over 11.9 g (0.19 mole) of dry, powdered potassium cyanide (Fisher), and the procedure continued as in Method I. Glc analysis (3% SE 30, 5' x ¼", 90°C) gave a $t_{½}$ of 7 hr, a $t_{completion}$ of 25 hr, and ca. 33% maximum yield (occurring after 7 hr) of

suspected monocyanated product, 1-bromo-3-cyanopropane. Work-up was as in the synthesis of 1-cyanohexane, Method I, and gave 4.13 g (97%) of 1,3-dicyanopropane. Analysis compared to that of the product isolated in Method I.

The procedure was repeated several times under varying conditions. The first modification consisted of repeating the reaction at ambient temperature. Glc analysis (5% TCEPE, 10' x ¼", 117°C) gave a $t_{\frac{1}{2}}$ of 10.5 hr and a $t_{completion}$ of 48 hr. A 95% yield of 1,3-dicyanopropane was isolated. In the second modification, 0.1 mole equivalent (based on potassium cyanide) of dry, powdered potassium chloride was employed with the system at reflux. Glc analysis (3% SE 30, 5' x ¼", 100°C) showed product peaks (other than 1,3-dicyanopropane) forming and disappearing during the course of the reaction, 2 at retention times less than 1,3-dibromopropane, and 1 intermediate between starting material and 1,3-dicyanopropane. Glc analysis also gave a $t_{completion}$ of 25 hr, and a yield of ca. 100% of 1,3-dicyanopropane. The final modification in the procedure employed benzene instead of acetonitrile as the solvent, both at reflux and at ambient temperature. For the ambient system, glc analysis (5% TCEPE, 10' x ¼", 117°C) showed a $t_{\frac{1}{2}}$ of 10 hr, a $t_{completion}$ of 46 hr, and a yield of ca. 100% of 1,3-dicyanopropane. For the reflux system, analysis with the same glc column gave a $t_{\frac{1}{2}}$ of 12 hr, and a yield of ca. 100% of 1,3-dicyanopropane.

1,3-Dicyanopropane, Method III. A total of 7.08 g (0.045 mole) of 1-bromo-3-chloropropane (Eastman) were placed in a 25-ml volumetric flask, followed by enough 0.185 M stock solution of 18-crown-6 in acetonitrile (ca. 1.0 g (0.0038 mole)) to dilute the volume to the mark. The final solution (1.8 M in reactant and ca. 0.15 M in crown) was poured over 11.71 g (0.18 mole) of dry, powdered potassium cyanide (Fisher), and the mixture refluxed with vigorous stirring. Glc analysis (3% SE 30, 5' x ¼", 90°C) showed the formation and disappearance of 3 peaks (other than that of product) during the course of the reaction, 1 at a shorter retention time than starting material and 2 at retention times between that of starting material and 1,3-dicyanopropane. Glc analysis also showed a $t_{\frac{1}{2}}$ of 1 hr, a $t_{completion}$ of 30 hr, and a yield of ca. 100% of 1,3-dicyanopropane. The product peak in the glc analysis of the final solution had the same retention time as commercial 1,3-dicyanopropane (K & K Lab.).

A modification of the procedure was incorporated to isolate and characterize the intermediate products that were detected by glc analysis. The reaction was run as in the synthesis of 1,3-dicyanopropane above, with 7.07 g (0.045 mole) of 1-bromo-3-chloropropane, and the mixture refluxed for 8 hr. The solution was worked-up as in the synthesis of 1-cyanohexane, Method I. Distillation gave 4 fractions boiling between 55-115°C at 25 mm. Glc analysis (3% SE 30, 5' x ¼", 85°C) showed 4 compounds to be present in the fractions

in varying proportions. The compounds were designated as (from lowest to highest glc retention time) 1,3-dichloropropane, 1-bromo-3-chloropropane, 1,3-dibromopropane, and 1-halo-3-cyanopropane. The first 3 compounds had the same retention times as the corresponding commercial chemicals (Eastman). The low-boiling fractions consisted mainly of 1,3-dichloropropane and 1-bromo-3-chloropropane, and the high boiling fractions were rich in 1,3-dibromopropane and 1-halo-3-cyanopropane (lit.[457-459] bp's were as follows (all at 760 mm): 1,3-dichloropropane, 120°C; 1-bromo-3-chloropropane, 141°C; 1,3-dibromopropane, 167°C; 1-chloro-3-cyanopropane, 195-197°C; and 1-bromo-3-cyanopropane, 205-207°C). Nmr analysis of the mixtures (neat or $CHCl_3$, external TMS) showed peaks at 3.68 ppm (merged triplets, $CH_2\underline{CH_2}BR$ and $CH_2\underline{CH_2}Cl$) and at 2.12 ppm (m, $CH_2(X)\underline{CH_2}CH_2(X)$) in all of the fractions, and an additional absorption at 2.75 ppm (t, $CH_2\underline{CH_2}CN$) in the higher-boiling fractions. From glc peak areas and the total weight of the fractions, it was determined that the products were isolated in the following amounts and yields: 1,3-dichloropropane, 1.9 g (7.5%); 1-bromo-3-chloropropane, 0.6 g (11% of starting material recovered); 1,3-dibromopropane, 1.2 g (23%); and 1-halo-3-cyanopropane, 0.3 g (possible range of 4.5% (if 100% 1-bromo-3-cyanopropane) to 6.2% (if 100% 1-chloro-3-cyanopropane)). The exact composition of the 1-halo-3-cyanopropane was uncertain, i.e., the relative percentages of 1-bromo- and 1-chloro-3-cyanopropane could not be discertained from glc and nmr data. No attempt was made to continue

distillation of the higher-boiling pot remains, which were shown by nmr analysis ($CHCl_3$, external TMS) to consist of 18-crown-6 and 1,3-dicyanopropane: 3.58 (sharp s, $OC\underline{H}_2C\underline{H}_2O$ of crown), 2.55 (4H, t, $C\underline{H}_2(CN)CH_2$), and 2.00 (2H, m, CH_2-$(CN)C\underline{H}_2$) ppm.

1,4-Dicyanobutane, Method I. Into a 25-ml volumetric flask were placed 5.75 g (0.045 mole) of 1,4-dichlorobutane (Fisher), followed by sufficient 0.185 M stock solution of 18-crown-6 in acetonitrile (ca. 0.95 g (0.0036 mole)) to dilute the volume to the mark, giving a final concentration of 1.8 M in reactant and ca. 0.14 M in crown. The prepared solution was poured over 11.8 g (0.18 mole) of dry, powdered potassium cyanide, and the system brought to reflux with rapid stirring. Glc analysis (10% Carbowax 20M, 5' x 1/8", 92°C) gave a $t_{\frac{1}{2}}$ of 0.2 hr and a $t_{completion}$ of 0.7 hr. Nmr analysis (CH_3CN, external TMS) revealed the disappearance of the $C\underline{H}_2$-$(Cl)CH_2$ triplet at 3.35 ppm, the appearance of the $C\underline{H}_2(CN)CH_2$ triplet at 2.30 ppm, and (in conjunction with glc) no side-products. Work-up as in the synthesis of 1-cyanohexane, Method I, produced 4.61 g (95%) of 1,4-dicyanobutane as a colorless liquid: bp 89-93°C (0.05 mm) (lit.[460] bp 180°C at 20 mm); nmr peaks (neat, external TMS) at 2.35 (4H, t, $C\underline{H}_2(CN)CH_2$) and 1.56 (4H, m, $CH_2(CN)C\underline{H}_2CH_2$) ppm; ir absorptions (neat, external TMS) at 2950 (C-H), 2240 (C≡N), and 1450 (CH_2) cm^{-1}; and mass spectral peaks with relative abundances at m/e 108 (parent ion, magnified) 68 (95%), 55 (59%), 43 (98%),

41 (100%), 39 (41%), and 27 (35%). The glc, ir, and nmr analyses of the isolated product corresponded to those of commercial 1,4-dicyanobutane (Aldrich). The procedure repeated at ambient temperature gave by glc analysis (10% Carbowax 20M, 5' x 1/8", 92°C) a $t_{\frac{1}{2}}$ of 8 hr and a $t_{completion}$ of 75 hr. Work-up gave 4.2 g (86%) of 1,4-dicyanobutane.

The method was duplicated at reflux except that no 18-crown-6 was used. Glc analysis (3% SE 30, 5' x ¼", 85°C) showed a $t_{\frac{1}{2}}$ of 25 hr and a peak intermediate in retention time to that of starting material and 1,4-dicyanobutane that increased in area during the initial course of the reaction and then decreased. The reaction was halted after 45 hr, and the mixture worked-up as in the synthesis of 1-cyanohexane, Method I. Two fractions were obtained on distillation, the first at bp 45-52°C (0.12 mm) and the second at 90-98°C (0.12 mm). Nmr analysis of the first fraction (neat, external TMS) disclosed peaks at 3.65 (2H, t, $C\underline{H}_2(Cl)CH_2$), 2.40 (2H, t, $C\underline{H}_2(CN)CH_2$), and 1.85 (4H, m, $CH_2(X)C\underline{H}_2CH_2$) ppm, confirming the compound to be 1-chloro-4-cyanobutane. Glc analysis gave the same retention time for the isolated 1-chloro-4-cyanobutane (1.6 g, 30%) as for the observed intermediate peak in the reaction mixture. Nmr analysis (neat, external TMS) as well as glc analysis (3% SE 30, 5' x ¼", 110°C) of the second fraction (1.6 g (33%)) was identical to that of commercial 1,4-dicyanobutane (Aldrich).

1,4-Dicyanobutane, Method II. Into a 25-ml volumetric flask were placed 9.73 g (0.045 mole) of 1,4-dibromobutane

(Eastman), and the volume diluted to the mark with 0.185 M stock solution of 18-crown-6 in acetonitrile (ca. 0.93 g (0.0035 mole)) to give a final concentration of 1.8 M in reactant and ca. 0.14 M in crown. The solution was placed over 11.6 g of dry, powdered potassium cyanide (Fisher), the mixture refluxed with vigorous stirring, and glc analysis (10% Carbowax 20M, 5' x 1/8", 120°C) utilized to show a $t_{\frac{1}{2}}$ of 6.5 hr and a $t_{completion}$ of 14 hr. No side-product peaks were observed in the chromatograph, and nmr analysis (CH_3CN, external TMS) of the product mixture showed the disappearance of the $\underline{CH_2}(Br)CH_2$ triplet at 3.25 ppm, the appearance of the $\underline{CH_2}(CN)CH_2$ triplet at 2.20 ppm, and no impurity peaks. An identical reaction run at ambient temperature gave on glc analysis of $t_{\frac{1}{2}}$ of 11 hr and a $t_{completion}$ of 57 hr.

Two modifications of the procedure were run. In the first, the reaction was repeated at reflux but with 18-crown-6 omitted. Glc analysis (3% SE 30, 5' x ¼", 110°C) demonstrated a $t_{\frac{1}{2}}$ of 24 hr and a peak intermediate in retention time between starting material and 1,4-dicyanobutane that appeared during the course of the reaction and then decreased in area. After 49 hr all of the 1,4-dibromobutane had reacted, and by relative peak areas, the products consisted of a ca. 87% yield of 1,4-dicyanobutane and a ca. 8% yield of 1-chloro-4-cyanobutane. In the second modification, the original reaction with crown was repeated, but the refluxing was halted and the reaction mixture worked-up after 7.7 hr. Distillation gave 4

fractions collected between 25°C and 102°C (0.12 mm) that contained varying amounts of 1,4-dibromobutane, 1-bromo-4-cyanobutane, and 1,4-dicyanobutane by glc analysis. By nmr analysis (neat or $CHCl_3$, external TMS), the lower-boiling fractions consisted mainly of starting material (3.48 (4H, t, $C\underline{H}_2(Br)CH_2$) and 2.05 (4H, m, $CH_2(Br)C\underline{H}_2$) ppm), the middle fractions mainly of 1-bromo-4-cyanobutane (3.65 (2H, t, $C\underline{H}_2(Br)CH_2$), 2.60 (2H, t, $CH_2C\underline{H}_2(CN)$), and 2.05 (4H, m, $CH_2(X)C\underline{H}_2CH_2$) ppm), and the higher-boiling fractions predominately of 1,4-dicyanobutane (2.60 (4H, t, $C\underline{H}_2(CN)CH_2$) and 2.00 (4H, m, $CH_2(CN)C\underline{H}_2CH_2$) ppm). The fraction collected at bp 48-60°C (0.12 mm) contained by nmr integration analysis 82% of 1-bromo-4-cyanobutane and 18% of 1,4-dibromobutane. From integration analyses and the weights of all the fractions, it was determined that 2.4 g (46%) of 1-bromo-4-cyanobutane and 1.25 g (26%) of 1,4-dicyanobutane were isolated.

1,4-Dicyanobutene. Into a 25-ml volumetric flask were placed 5.62 g (0.045 mole) of a mixture of cis- and trans-1,4-dichloro-2-butene (Aldrich), and the volume diluted to the mark with 0.185 M stock solution of 18-crown-6 in acetonitrile (ca. 1.0 g (0.0038 mole)) to give a final concentration of 1.8 M in reactant and ca. 0.15 M in crown. The solution was placed in the reaction flask and cooled to 10°C with an ice bath. With vigorous stirring, 11.7 g (0.18 mole) of dry, powdered potassium cyanide (Fisher) was added to the cold solution. The reaction temperature was kept below 20°C. Glc

analysis (3% SE 30, 5' x ¼", 65°C) showed the formation and area growth of 2 overlapping product peaks at a retention time less than that of starting material. When the overlapping peaks began to decrease in area, the reaction was stopped (3 hr), and the solution filtered (gravity) into a stirred 2-layer system of 75 ml of methylene chloride and 75 ml of distilled water. The layers were stirred for 10 min, separated, and the methylene chloride solution dried (anhydrous magnesium sulfate, 12 hr). The solvent was removed by distillation utilizing a vigreux column, and the low-boiling reaction products distilled at atmospheric pressure. Glc analysis (3% SE 30, 5' x ¼", 65°C) showed that the fractions boiling in the range 71-88°C (760 mm) contained (in addition to acetonitrile) the starting material peak and the overlapping peaks observed during the course of reaction. Nmr spectra (neat, external TMS) of the fraction exhibited the acetonitrile peak (1.85 ppm, sharp s) and peaks at 6.65 (m, CH(X)=C<u>H</u>CH), 5.40 (m, C<u>H</u>(X)=CH), and 3.80 (m, CH=C<u>H</u>$_2$) ppm. The low-boiling product was collected by glpc (3% SE 30, 5' x ¼", 55°C) as a colorless liquid and in sufficient quantity for mass spectral analysis. The overlapping peaks were collected as 1 fraction. Mass spectral analysis gave major peaks with relative abundances at <u>m/e</u> 79 (parent ion, 100%), 52 (52%), and 27 (44%). The mass spectrum and nmr analysis were consistent with a mixture of <u>cis</u>-, <u>trans</u>-1-cyano-1,3-butadiene.

The high-boiling pot remains partially solidified to

crystalline rods on sitting. The light tan solid (mp 90-90.7°C) was filtered and the filtrate saved for distillation. Nmr analysis ($CDCl_3$, external TMS) of the crystalline material showed it to consist mainly of 18-crown-6 (3.75 ppm, strong singlet, $OC\underline{H}_2C\underline{H}_2O$), with additional peaks at 7.40 (m, $CH(X)=C\underline{H}CH_2$), 5.98 (m, $C\underline{H}(X)=CH$ or $CH_2(X)C\underline{H}=CH$), 3.05 (m, $CH_2C\underline{H}(X)$ and $C=CHC\underline{H}_2CH_2(X)$), and 2.35 (m, $C\underline{H}_2(X)CH=CH$) ppm. The solid was dissolved in methylene chloride, and the solution analyzed by glc (3% SE 30, 5' x ¼", 131°C). The nitrile components eluted as 2 sets of overlapping peaks at t_{ret} 1.1 min and 3.0 min.

Distillation of the filtrate began at bp 120-125°C (2.0 mm); however, the distillate solidified and plugged the condenser path (spherulytic, white crystals), and the process had to be discontinued. The mp of the solid depended on which part of the distillation path that the material was located, varying from 70-71°C (cow fraction divider) to 55-56.5°C (condenser). Nmr analyses were the same for all segments of the distillate, but showed different proportions of 18-crown-6, depending again on the location of the analysed material in the distillation path. The nmr spectrum ($CDCl_3$, external TMS) gave the sharp crown singlet at 3.75 ppm, and 5 distinct absorption bands due to the various nitrile compound protons. By correlation with the literature[341], 3 of the bands were assigned to cis-, trans-1,4-dicyano-1-butene: 6.50 (1H, complex m, $CH(X)=C\underline{H}CH_2$), 5.52 (1H, d, $C\underline{H}(X)=CH$),

and 2.57 (4H, m, $CH_2\underline{CH}_2(X)$ and $CH{=}CH\underline{CH}_2CH_2(X)$) ppm. Likewise, the remaining 2 bands were correlated with those reported for 1,4-dicyano-2-butene: 5.92 (2H, m, $CH_2(X)\underline{CH}{=}CH$) and 3.32 (4H, m, $\underline{CH}_2(X)CH{=}CH$) ppm[357]. The relative proportions of 1-butene and 2-butene also varied with the location of the material in the distillation path. Ir spectra (neat, NaCl plates) of the uncrystallized receiver distillate gave several peaks assignable to the nitrile compounds (crown was also present): 2240 and 2215 (C≡N), 1637 (shoulder, trans C=C) and 1625 (cis C=C), and 969 (trans C=C) and 743 (cis C=C) cm^{-1} (similar to lit.[341] values for cis,-trans-1,4-dicyano-1-butene). Glc analyses (3% SE 30, 5' x ¼", 131°C) were the same for all samples of the material, showing the two sets of coalesced peaks noted for the crystals isolated from the high-boiling pot remains. Two minor but distinct peaks were disclosed at relatively long retention times. The material isolated on distillation was collectively dissolved in methylene chloride and the components separated and isolated by glpc (3% SE 30, 5' x ¼", 120°C). The procedure yielded a brown-tint, transparent liquid (Compound I, set of overlapping peaks of shortest t_{ret} collected as 1 fraction), a white, crystalline solid (Compound II, first peak of overlapping peaks with longest t_{ret}, mp 70-72°C), a colorless liquid (Compound III, second peak of set with longest t_{ret}), another crystalline solid (Compound IV, minor component collected at ca. t_{ret} 21 min, mp 78-79°C (crystalline transition at 67-68°C)), and a fine

solid (Compound V, minor component collected at ca. t_{ret} 29 min, insufficient quantity isolated for mp determination). Mass spectrometry was used to analyze Compounds I-III, giving the following major peaks (m/e) with relative abundances: 1) Compound I: 106 (parent ion, 100%), 104 (14%), 79 (31%), 77 (23%), 66 (100%), 54 (17%), 52 (33%), and 39 (39%); 2) Compound II: 106 (39%), 104 (28%), 79 (25%), 77 (53%), 66 (100%), 54 (12%), 52 (21%), and 39 (38%); and 3) Compound III: 106 (53%), 104 (67%), 79 (36%), 77 (98%), 66 (100%), 54 (15%), 52 (41%), and 39 (51%). The mass spectral analyses supported the nmr and ir analyses, the glc retention times, and the mp (where applicable) in identifying Compound I to be a cis-, trans-1,4-dicyano-1-butene mixture (lit.[342] bp (mixture) 122-132°C (3 mm), reported to be a liquid at room temperature[317]), and Compounds II and III to be trans- (Compound II) and cis- (Compound III) 1,4-dicyano-2-butene (lit.[461] bp (mixture) 113-117°C (1 mm); lit.[461] mp (mixture) 73-75°C; trans- isomer a solid at 25°C[257]).

Mass spectral analyses of the 2 minor components collected by glpc gave major peaks (m/e) with relative abundances as follows: 1) Compound IV: 158 (parent ion, 7%), 131 (24%), 92 (13%), 79 (100%), 65 (10%), 52 (27%), and 39 (14%); 2) Compound V: 158 (parent ion, 10%), 131 (15%), 92 (15%), 79 (100%), 65 (12%), 52 (38%), and 39 (22%). The mass spectral analyses, along with the long glc t_{ret} exhibited by the compounds, suggested that they were positional isomers of tetracyanobutane.

2-Cyanobutane. Into a 25-ml volumetric flask were placed 6.85 g (0.050 mole) of 2-bromobutane (Eastman) and the solution brought to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 0.93 g (0.0035 mole)) in acetonitrile, giving a final concentration of 2.0 M in reactant and ca. 0.14 M in crown. The solution was poured over 6.0 g (0.093 mole) of dry potassium cyanide (Fisher), refluxing was begun with vigorous stirring, and the course of the reaction followed by glc analysis (5% TCEPE, 10' x ¼", 62°C). Glc gave a $t_{½}$ of 16 hr, a $t_{completion}$ of 34 hr, and a yield of 2-cyanobutane of 70%. Nmr analysis (CH_3CN, external TMS) disclosed the disappearance of the $CH_3C\underline{H}(Br)CH_2$ multiplet at 3.95 ppm and the appearance of the $CH_3C\underline{H}(CN)CH_2$ peak at 2.40 ppm. The black, opaque mixture was filtered (gravity), poured into 125 ml of distilled water, and the aqueous solution extracted with 4-115 ml aliquots of ethyl ether. The combined extracts were dried (anhydrous magnesium sulfate, 12 hr), the solution filtered, (gravity), and the ethyl ether (lit.[462] bp 34.6°C (760 mm)) and the bulk of the acetonitrile (lit.[463] bp 80°C (760 mm)) removed by distillation at atmospheric pressure with aid of a vigreux column. Continued distillation rendered 3 fractions (colorless liquids) collected between 85°C and 122°C (760 mm). A significant amount of tarred material remained in the distillation pot. Glc analyses (3% SE 30, 5' x ¼", 50°C) of the fractions revealed that apparently an azeotrope had been formed between the 2-cyanobutane and the

acetonitrile, and that the 2 were present in varying amounts in all but the final fraction obtained (consisting of pure 2-cyanobutane, bp 122°C (760 mm)). From the weights of the fractions and the relative peak areas of the 2 components, it was determined that 1.5 g (37%) of 2-cyanobutane had been isolated: bp 122°C at 760 mm (lit.[464] bp 125-126°C (760 mm)); nmr peaks (neat, external TMS) at 2.38 (1H, m, $CH_3C\underline{H}(X)CH_2$), 1.33 (2H, m, $CH(X)C\underline{H}_2CH_3$), 0.95 (3H, d, $C\underline{H}_3CH(X)$), and 0.95 (3H, t, $CH_2C\underline{H}_3$) ppm; ir absorptions (neat, NaCl plates) at 2960 (C-H), 2230 (C≡N), 1455 (CH_2), 1380 (CH_3), and 1327 (CH) cm^{-1};and mass spectra peaks with relative abundances at m/e 82 (parent ion - 1 H, 2%), 55 (100%), 41 (68%), and 29 (42%).

The procedure was repeated, except that C_6H_6 was substituted for CH_3CN as the refluxing solvent. Glc analysis (5% TCEPE, 10' x ¼", 62°C) revealed a $t_{½}$ of 62 hr and a ca. 43% yeild of 2-cyanobutane at time of stoppage (66 hr), i.e., the reaction was not allowed to proceed to completion. A monitor of the reaction by nmr (CH_3CN, external TMS), utilizing the 18-crown-6 singlet as an internal integration standard in relation to the decreasing $CH_3C\underline{H}(Br)CH_2$ band area, gave a comparable $t_{½}$ of 55 hr.

2-Cyanooctane, Method I. Into a 25-ml volumetric flask were placed 9.65 g (0.050 mole) of 2-bromooctane (Eastman), and the volume raised to the mark with a 0.185 M stock solution of 18-crown-6 (0.79 g (0.0030 mole)) in acetonitrile to give

a final concentration of 2.0 M in reactant and ca. 0.12 M in crown. The solution was placed over 7.7 g (0.12 mole) of dry, powdered potassium cyanide (Fisher) and brought to reflux with vigorous stirring. Glc analysis (3% SE 30, 5' x ¼", 85°C) disclosed a $t_{\frac{1}{2}}$ of 15 hr, a $t_{completion}$ of 70 hr, and 2 product peaks at t_{ret} 0.63 min (17% yield of octenes) and at t_{ret} 5.25 min (62% yield of 2-cyanooctane). The t_{ret} of 2-bromooctane was 4.50 min. Nmr analysis (CH_3CN, external TMS) showed the disappearance of the $CH_3\underline{C}H(Br)CH_2$ peak (5.30 ppm), the appearance of the $CH_3\underline{C}H(CN)CH_2$ peak (2.50 ppm), and the appearance and area growth of a complicated multiplet (5.20 ppm, olefin proton region). The dark black, opaque solution was filtered (gravity), placed in 50 ml of distilled water, and the aqueous solution extracted with 4-75 ml aliquots of methylene chloride. The combined extracts were dried (anhydrous magnesium sulfate, 5 hr), filtered (gravity), and the methylene chloride (lit.[465] bp 40-41°C (760 mm)) and the bulk of the acetonitrile (lit.[463] bp 80°C (760 mm)) removed by distillation. Attempted distillation of the low-boiling product at both atmospheric pressure and aspirator vacuum was unsuccessful due to excessive foaming of the mixture as the bp was approached. Low-temperature glc analysis of the mixture (3% SE 30, 5' x ¼", 35°C) revealed that the volatile product was actually composed of 3 compounds with a distinct peak at t_{ret} 5.5 min (23% of the mixture) and a pair of overlapping peaks at t_{ret} 6.0 min and 6.3 min (77% (combined)

of the mixture). The low-temperature chromatogram overlapped in appearance and t_{ret} to that of an isolated and characterized mixture of 1-octene and cis-, trans-2-octene (supplied by Dr. H. P. Harris[106]). Nmr spectra (CH_3CN, external TMS) of the product solution showed a broad band containing 5 distinct peaks at 5.20 ppm that overlapped with the alkene proton band of the isolated octene mixture[106].

Continued distillation of the concentrated product mixture afforded 3.9 g (56%) of 2-cyanooctane as a clear, colorless liquid (a substantial amount of tarred material remained in the distillation pot): bp 65-66°C at 2.0 mm (lit.[466] bp 55°C (1.0 mm) for 1-cyanooctane); nmr bands (neat, external TMS) at 2.35 (1H, m, $CH_3\underline{C}H(X)CH_2$), 1.52 (10H, m, internal $C\underline{H}_2$), 1.17 (3H, d, $C\underline{H}_3CH(X)$), and 1.10 (3H, t, $CH_2C\underline{H}_3$) ppm; ir absorptions (neat, NaCl plates) at 2930 (C-H), 2240 (C≡N), 1460 (CH_2), 1375 (CH_3), and 1325 (CH) cm^{-1}; and mass spectral peaks with relative abundances at m/e 138 (parent ion - 1 H, 2%), 124 (13%), 110 (36%), 96 (100%), 69 (32%), 83 (47%), 55 (79%), 43 (94%), 41 (83%), 29 (43%), and 27 (30%).

2-Cyanooctane, Method II. The procedure was as in Method I, except that 7.43 g (0.050 mole) of 2-chlorooctane (Aldrich) was substituted for the 2-bromooctane. Monitoring of the course of reaction by glc (3% SE 30, 5' x ¼", 90°C) showed a $t_{½}$ of 59 hr and a yield after 220 hr of 78% of 2-cyanooctane and 3% of octene. Starting material (7% of mixture

by glc) remained after 244 hr, at which time the reaction was halted. Low-temperature glc analysis (3% SE 30, 5' x ¼", 35°C) of the olefin product corresponded to that reported in Method I.

Attempted Synthesis of Cyclohexyl Cyanide. Into a 25-ml volumetric flask were placed 7.34 g (0.045 mole) of cyclohexyl bromide (Eastman), and the volume diluted to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 0.88 g (0.0033 mole)) in acetonitrile to give a final concentration of 1.8 M in reactant and ca. 0.13 M in crown. The solution was poured over 6.7 g (0.11 mole) of dry, powdered potassium cyanide, and the course of reaction followed by glc (10% Carbowax 20M, 5' x 1/8", 92°C) and nmr (CH_3CN, external TMS). No glc peak appeared in the expected region for cyclohexyl cyanide, although the starting material decreased steadily in peak area with time. After 54 hr, 46% of the cyclohexyl bromide had reacted. Nmr analysis showed the decrease in area of the $CH_2\underline{CH}(Br)CH_2$ band at 4.05 ppm, no formation of the $CH_2\underline{CH}(CN)CH_2$ peak in the expected region (2-3 ppm), and the formation and growth with time of the cyclohexene proton absorption band (5.43 ppm, broad, multi-spiked band). The latter corresponded in appearance to that of an isolated, characterized sample of cyclohexene (nmr spectrum supplied by Dr. H. P. Harris[106]). As no side-product bands were evident in the nmr or glc analyses, the yield of cyclohexene was equated with the decrease in starting material (46%) at the time of stoppage (54 hr).

The reaction was repeated, except that 5.34 g (0.045 mole) of cyclohexyl chloride (Aldrich) was substituted for the cyclohexyl bromide. Glc monitoring of the reaction (3% SE 30, 5' x ¼", 65°C) revealed again that no cyclohexyl cyanide was formed and that low-boiling cyclohexene (lit.[467] bp 83°C (760 mm)) with t_{ret} 0.25 min (eluting just after the acetonitrile peak) was produced. After 123 hr (stoppage point), the chromatogram showed that 65% of the starting material remained and that the yield of the cyclohexene had reached 31%.

Attempted Preparation of 2-Chlorobenzonitrile. Into a 25-ml volumetric flask were poured 6.64 g (0.045 mole) of o-dichlorobenzene (Fisher), and the volume brought to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 0.97 g (0.0037 mole)) in acetonitrile to give a final concentration of 1.8 M in reactant and ca. 0.15 M in crown. The liquid was placed over 11.8 g (0.18 mole) of dry, powdered potassium cyanide (Fisher), refluxing begun with vigorous stirring, and the reaction monitored by glc (3% SE 30, 5' x ¼", 85°C). The glc analysis demonstrated that after 109 hr at reflux, the peak area of the starting material had not decreased, and that no product peak had formed. Nmr spectra (CH_3CN, external TMS) of the pink-tinted final solution exhibited the same pattern as had the starting solution, with no new bands due to product formation.

Attempted Preparation of 4-Nitrobenzonitrile. Into a 25-ml volumetric flask were placed 7.09 g (0.045 mole) of solid

4-chloronitrobenzene (Eastman), and the volume raised to the mark and the solid dissolved with a 0.185 M stock solution of 18-crown-6 (ca. 0.98 g (0.0037 mole)) in acetonitrile to give a final concentration of 1.8 M in reactant and ca. 0.15 M in crown. The solution was poured over 6.0 g (0.93 mole) of dry, powdered potassium cyanide (Fisher), refluxing begun with vigorous stirring, and the reaction monitored by glc (3% SE 30, 5' x ¼", 120°C). Analysis showed that 82% of the starting material remained after 80 hr at reflux, and that no peak had formed at the retention time range expected for 4-nitrobenzonitrile. After 101 hr, the reaction was halted, the black, opaque solution filtered (aspirator suction), and the solution worked-up as in the synthesis of 1-cyanohexane, Method I. A tar-like substance was present in the solution that was only sparingly soluble in methylene chloride, and thus the continuous extractor was operated for 48 hr. The black, tar-like remains partially crystallized on sitting after work-up. The solid was recrystallized several times from a 50% acetic acid-water mixture after the method of 4-nitrobenzonitrile purification of Miller[433]. A total of 3.8 g of a yellow-tan, fine solid was isolated that had a mp of 81.5-82°C, indicating it to be recovered (54%) 4-chloronitrobenzene (lit.[468] mp of 4-chloronitrobenzene, 83°C; lit.[433] mp of 4-nitrobenzonitrile, 146-147°C).

Attempted Preparation of 2,4-Dinitrobenzonitrile. Into a 25-ml volumetric flask were placed 9.12 g (0.045 mole) of

solid 2,4-dinitrochlorobenzene (Eastman), and the volume raised to the mark and the solid dissolved with a 0.185 M stock solution of 18-crown-6 (ca. 0.93 g (0.0035 mole)) in acetonitrile to give final concentrations of 1.8 M in reactant and ca. 0.14 M in crown. The solution was poured over 6.0 g (0.092 mole) of dry, powdered potassium cyanide, at which time the liquid immediately turned an opaque, dark green in color. Refluxing was begun with vigorous stirring and monitoring of the reaction attempted by glc (3% SE 30, 5' x ¼", 160°C). After 1 hr at reflux, the solution became so viscous that it could not be drawn up into the syringe needle accurately, and the glc analysis had to be discontinued. The reaction was allowed to proceed for an additional 3 hr, the opaque solution filtered, and the solvent removed (rotary evaporation, aspirator pressure). A black, tar-like material remained that was sparingly soluble in methylene chloride, but dissolved readily in acetone. The tar-like liquid remaining after acetone evaporation (air) was not crystallizable. No 2,4-dinitrocyanobenzene was isolated.

The attempted synthesis was repeated, except that 8.38 g (0.045 mole) of 2,4-dinitrofluorobenzene (PCR, Inc.) was substituted for the 2,4-dinitrochlorobenzene, and the reaction temperature was altered in that the pot containing the potassium cyanide was cooled in an ice bath before addition of the cold reactant-crown solution. The liquid turned an opaque, dark green upon contact with the salt, the reaction

temperature rose to 15°C due to an exothermic reaction, and then stabilized at 0-10°C after 10 min. Glc analysis (3% SE 30, 5' x ¼", 170°C) indicated that no reaction had taken place after 2 hr at 0-10°C. The ice bath was replaced with a water bath, and the reaction temperature was raised and held at 20-25°C. After an additional 21 hr at 20-25°C, the glc showed that all of the 2,4-dinitrofluorobenzene had reacted, but that no peak had appeared in the expected retention time region for 2,4-dinitrobenzonitrile (up to t_{ret} 11 min monitored). The cold solution was filtered (aspirator suction) and worked-up as in the synthesis of 1-cyanohexane, Method I. A tar-like, uncrystallizable liquid was obtained that was the same in appearance as the material obtained with 2,4-dinitrochlorobenzene. No 2,4-dinitrobenzonitrile was isolated.

Attempted Synthesis of Benzoyl Cyanide. Into the dry reaction flask were placed 6.1 g (0.093 mole) of dry, powdered potassium cyanide followed by 21 ml of a 0.185 M stock solution of 18-crown-6 (ca. 1.0 g (0.0039 mole)) in acetonitrile. The solution was stirred over the dried salt for 15 min, and 6.33 g (0.045 mole) of benzoyl chloride (Fisher) was added in one portion to give a final concentration of 1.8 M in reactant and 0.15 M in crown. The reaction was run at ambient temperature for 2 hr, the solution filtered, the acetonitrile removed (rotary evaporation, aspirator pressure), and the soluble remains dissolved in 300 ml of methylene chloride.

A layer of distilled water (300 ml) was placed over the organic layer, and the 2-phase system stirred for 1 hr. The red-black, opaque organic layer was separated, dried (anhydrous magnesium sulfate), filtered (aspirator suction), and the solvent removed (rotary evaporation, aspirator pressure). Attempted distillation gave no definite bp at 0.1 mm (lit.[398] bp of benzoyl cyanide, 105°C (0.1 mm)), although some orange-tint, transparent liquid formed in the receiver and yellow, needle crystals solidified in the condenser (mp 105-109°C). Nmr spectra ($CDCl_3$, external TMS) of the receiver liquid showed complicated multiplets at 8.00 ppm (20 integration units, aromatic proton alpha to a substituent) and 7.40 ppm (65 integration units, aromatic protons beta or further removed from a substituent). Upon evaporation of the nmr solvent, the material crystallized into yellow needles (mp 117-120°C). Nmr analysis ($CDCl_3$, external TMS) disclosed a singlet at 12.50 ppm (7 integration units, COOH) and additional peaks at 8.40 ppm and 7.72 ppm (25 and 54 integration units, respectively, with assignments as above). Upon partial evaporation of the solvent, uniform yellow needle crystals were obtained (mp 110-111.5°C). Two possible compounds present were benzoic acid (lit.[469] mp 122.4°C) and α-benzolyloxy-α-phenylmalononitrile (the dimer of benzoyl cyanide, lit.[398] mp 94-95°C). No benzoyl cyanide (lit.[398] mp 30-32°C) was isolated.

Hydrocyanation Reaction (1,2-Dicyanopropane)

Into a 25-ml volumetric flask were placed 3.03 g (0.045 mole) of methacrylonitrile (Eastman), and the volume raised to the mark with a 0.185 M stock solution of 18-crown-6 (ca. 1.0 g (0.0039 mole)) in acetonitrile. The crown-reactant solution was combined with 4.42 g (0.052 mole) of acetone cyanohydrin (J. T. Baker Chem. Co.) to give final approximate solution concentrations of 1.5 M in methacrylonitrile, 0.13 M in crown, and 1.8 M in acetone cyanohydrin. The reaction solution was placed over 0.32 g (0.005 mole) of dry, powdered potassium cyanide (Fisher), refluxing begun with vigorous stirring, and the disappearance of methacrylonitrile followed by glc (3% SE 30, 5' x ¼", 50°C). The analysis revealed a $t_{\frac{1}{2}}$ of 0.3 hr and a $t_{completion}$ of 0.6 hr. Nmr analysis (CH_3CN, external TMS) showed no remaining olefin proton band at 5.65 ppm. The final solution contained a product that had a glc retention time slightly lower than that of commercial 1,3-dicyanopropane (K & K Lab.). The solution was filtered (aspirator suction) and worked-up as in the synthesis of 1-cyanohexane, Method I. On evaporation of the methylene chloride, the crystalline crown-1,2-dicyanopropane complex (mp 69-70.5°C) fell out of solution. The solid-liquid mixture was distilled after melting the solid in the distillation flask to give 3.89 g (92%) of 1,2-dicyanopropane as a colorless liquid: bp 68-71°C (0.15 mm); nmr peaks (neat, external TMS) at 3.05 (1H, m, $CH_3C\underline{H}(X)CH_2(X)$), 2.65 (2H, d, $CH(X)C\underline{H}_2(X)$), and 1.35

(3H, d, $C\underline{H}_3CH(X)$) ppm; ir absorptions (neat, NaCl plates) at 2975 (C-H), 2250 (C≡N), 1460 (CH_2), 1380 (CH_3), and 1330 (CH) cm^{-1}; and mass spectral peaks with relative abundances at m/e 94 (parent ion, magnified), 93 (6%), 66 (14%), 54 (100%), 41 (93%), 28 (51%), and 27 (34%). The reaction repeated at ambient temperature had proceeded to an approximate yield of 46% of 1,2-dicyanopropane (by the decrease of the methacrylonitrile glc peak area) after 189 hr.

The reaction was duplicated at reflux, but without 18-crown-6. Glc analysis showed a $t_{\frac{1}{2}}$ of 6 hr and a $t_{completion}$ of 15 hr. Work-up and distillation gave 4.3 g (77%) of 1,2-dicyanopropane. Nmr analysis (neat, external TMS) of the isolated product corresponded to that detailed above.

Cyanohydrin Formation Reactions

Cyclohexanone Cyanohydrin. Into a 25-ml volumetric flask were placed 1.0 g (0.0038 mole) of 18-crown-6, the solid dissolved with 15 ml of benzene, and 4.42 g (0.045 mole) of cyclohexanone (Eastman) added along with enough benzene to raise the volume to the mark. The solution was combined in the reaction flask with 3.39 g (0.040 mole) of acetone cyanohydrin (J. T. Baker Chem. Co.) to give final approximate concentrations of 1.6 M in acetone cyanohydrin, and 0.13 M in crown. Nmr spectra (C_6H_6, external TMS) of the mixture showed peaks at 4.50 (s, O$\underline{H}$ of acetone cyanohydrin), 3.05 (s, $OC\underline{H}_2C\underline{H}_2O$ of crown), 1.65 (m, $CH_2C\underline{H}_2C{=}O$), 1.00 (sharp s, $C\underline{H}_3$ of acetone cyanohydrin), and 1.00 (m,

ring $C\underline{H}_2$) ppm. Integration gave a crown hydrogen : acetone cyanohydrin hydroxyl hydrogen ratio of 2:1. Dry, powdered potassium cyanide (0.30 g, 0.0047 mole) was added, and the system brought to reflux and held with vigorous stirring for 2.7 hr. Nmr analysis (C_6H_6, external TMS) of the final solution (positions corrected, using the 18-crown-6 as an internal standard) disclosed peaks at 5.10 (s, $O\underline{H}$ of cyclohexanone cyanohydrin), 3.05 (sharp s, $OC\underline{H}_2C\underline{H}_2O$ of crown), 1.70 (m, $CH_2C\underline{H}_2C(X)_2$), 1.40 (sharp s, $C\underline{H}_3$ of acetone), and 1.13 (m, ring $C\underline{H}_2$) ppm. Integration gave a crown hydrogen to cyclohexanone cyanohydrin hydroxyl hydrogen ratio of 2:1, indicating a quantitative yield of cyclohexanone cyanohydrin. The solution was filtered (aspirator suction), washed with 75 ml of distilled water, and the water layer extracted with 3-50 ml aliquots of ethyl ether. The ether extracts were combined with the benzene layer, the mixture dried (anhydrous magnesium sulfate, 3 hr), the salt filtered (aspirator suction), and the low-boiling constituents removed by rotary evaporation (aspirator pressure). Nmr spectra ($CDCl_3$, external TMS) of the viscous, orange-red, transparent remains showed peaks for cyclohexanone cyanohydrin, residual 18-crown-6, and residual benzene, but no methyl singlet of acetone or the corresponding cyanohydrin. Distillation afforded 2.2 g of colorless liquid (bp 89-91^{o}C (1.0 mm)) in the receiver, and 2.5 g of colorless liquid in the oil pump cold trap (dry ice-acetone coolant bath). Analysis of the

receiver liquid identified it as cyclohexanone cyanohydrin (39% yield): bp 89-91°C at 1.0 mm (lit.[470] bp 109-113°C at 9 mm); nmr peaks ($CDCl_3$, external TMS) at 4.85 (broad s, O<u>H</u> of cyclohexanone cyanohydrin) and 1.65 (broad (0.9-2.6 ppm), multi-peaked band, ring C<u>H</u>$_2$) ppm; ir absorptions (neat, NaCl plates) at 3475 (O-H), 2925 (C-H), 2225 (C≡N), 1450 (CH_2), 1345 (OH), and 1090 (C-O) cm^{-1}; and mass spectral peaks with relative abundances at <u>m/e</u> 125 (parent ion, magnified), 98 (100%), 83 (29%), 55 (96%), 42 (75%), 39 (53%), and 27 (41%). The ir spectra also exhibited a weak absorption at 1695 cm^{-1} (C=O impurity). The liquid did not crystallize on sitting at room temperature (lit.[470] mp of cyclohexanone cyanohydrin, 34-36°C). Nmr analysis (neat, external TMS) of the cold-trap liquid revealed peaks at 2.13 (m, $CH_2C\underline{H}_2C$=O) and 1.65 (broad m, ring C<u>H</u>$_2$). The spectra corresponded closely to that of pure cyclohexanone (Eastman, lit.[471] bp 156°C at 760 mm), with only a minor absorption at 4.45 ppm due to residual cyanohydrin hydroxyl proton, and thus 57% of starting material was recovered on distillation of the crude cyclohexanone cyanohydrin.

Several modifications of the procedure were adopted. The reaction when repeated <u>without</u> 18-crown-6 furnished a 14% yield of cyclohexanone cyanohydrin and 70% of recovered cyclohexanone. When CH_3CN was substituted for C_6H_6 in the original procedure with crown, an 18% yield of cyclohexanone cyanohydrin was obtained.

Attempted Formation of Acetophenone Cyanohydrin. Into a 3-dram vial were placed 0.0672 g (0.00254 mole) of 18-crown-6, 0.36 g (0.0055 mole) of dry, powdered potassium cyanide, 4.7 ml of benzene, and a small Teflon-coated stirring bar. The vial was capped and the solution stirred vigorously for 1.5 hr at ambient temperature. The stirring bar was removed, the solid-liquid mixture separated by centrifugation, and the crown-"Naked" cyanide solution pipetted (bulb) into a second 3-dram vial containing 0.296 g (0.00247 mole) of acetophenone (Eastman). The approximate final concentrations were 0.49 M in acetophenone and 0.51 M in crown. Vigorous stirring was begun and continued for 30 seconds at ambient temperature, at which time an aliquot was removed and placed in an nmr tube. The tube was kept spinning in the probe, and numerous spectra taken at various intervals up to 1 hr (the original spectra calibrated by external TMS, 500 cps sweep width). Nmr analysis (C_6H_6, external TMS) of pure acetophenone had given a peak position for the methyl group (sharp s) at 1.50 ppm. In the reaction solution, only the methyl singlet of the acetophenone (1.50 ppm) and the crown singlet (2.90 ppm) were observed, with no new peak formation for the alkoxide anion methyl. A change to 250 cps sweep width failed to distinguish any new peaks. The solution from the nmr tube, along with the remainder in the vial, was poured into a 10-ml round bottom flask and refluxing begun with vigorous stirring. Samples were removed at intervals over a 6-day period for nmr analysis.

Again only the acetophenone methyl singlet was recorded. The benzene solution was then frozen (-10°C) in an nmr tube, and spectra recorded continuously until the solution returned to room temperature. As before, no new peak due to alkoxide anion formation was observed.

Attempted Formation of Benzaldehyde Cyanohydrin. Into a 3-dram vial were placed 0.339 g (0.00129 mole) of 18-crown-6, 0.182 g (0.00284 mole) of dry, powdered potassium cyanide, and 2.35 ml of benzene-d_6 (Aldrich). The vial was capped, the mixture stirred vigorously for 1.5 hr, the components separated by centrifugation, and the solution pipetted (bulb) off the salt into a second 3-dram vial containing 0.128 g (0.0012 mole) of benzaldehyde (Eastman). The approximate concentrations were 0.34 M in reactant and 0.36 M in crown. The solution was stirred for 1 min, partially transferred to a nmr tube, and the effect on the benzaldehyde proton peak (strong s, 4.75 ppm, $C_6H_5C(H)=O$ (external TMS)) monitored at ambient temperature for 30 min. No new peak due to alkoxide anion formation was observed, and no decrease in the peak area of the benzaldehyde proton occurred.

Decarbalkoxylation Reactions

Ethyl Phenylacetate. Into a 25-ml volumetric flask were placed 10.6 g (0.045 mole) of diethyl phenylmalonate (Aldrich), and the volume raised to the mark with a 0.181 M stock solution of 18-crown-6 (ca. 0.073 g (0.0028 mole)) in benzonitrile to give a final concentration of 1.8 M in reactant

and ca. 0.11 M in crown. The solution was poured over 6.3 g (0.097 mole) of dry, powdered potassium cyanide, and heating begun (80°C) with glc monitoring (3% SE 30, 5' x ¼", 162°C). The temperature was gradually raised until a reasonable rate of reaction was obtained (180°C). After 9 hr at 180°C, the glc analysis revealed approximately 16% of starting material remaining and a yield of ethyl phenylacetate of approximately 33%. The black, opaque solution was filtered (aspirator suction), placed in 150 ml of water, and the aqueous solution extracted with 4 -115 ml aliquots of methylene chloride. The combined extracts were dried (anhydrous magnesium sulfate, 3 hr), filtered (aspirator suction), and the methylene chloride removed (rotary evaporation, aspirator pressure). The benzonitrile was separated by distillation at aspirator pressure (bp 81-83°C at 25 mm (lit.[472] bp 190.7°C at 760 mm)). Continued distillation afforded 2.2 g (30%) of ethyl phenylacetate as a colorless liquid: bp 62-65°C at 0.5 mm (lit.[473] bp 120-121°C (20 mm)); nmr bands (neat, external TMS) at 6.80 (5H, s, $C_6\underline{H}_5CH_2$), 3.65 (2H, q, $OC\underline{H}_2CH_3$), 3.10 (2H, sharp s, $C_6H_5C\underline{H}_2$), and 0.70 (3H, t, $OCH_2C\underline{H}_3$) ppm; ir absorptions (neat, NaCl plates) at 3020 and 2975 (merged, aromatic C=C-H and alkane C-H, respectively), 1725 (C=O), 1600 and 1500 (aromatic C=C-H), 1450 (CH_2), 1375 (CH_3), 1250 and 1050 (C-O), and 700 (aromatic C=C-H) cm^{-1}; and mass spectral peaks at m/e 164 (parent ion, 100%), 119 (89%), 91 (83%), 65 (84%), 29 (55%), and 77 (29%). There

was evidence that an unidentified nitrile compound had been isolated as a minor side-product in the liquid: weak ir absorptions at 3600 (broad, O-H) and 2230 (sharp, C≡N), and mass spectral peak with relative abundance at m/e 192 (parent ion, 18%).

The reaction was repeated, except that 6.7 g (0.090 mole) of dry, powdered potassium chloride was substituted for the potassium cyanide. After 9 hr at 180°C, glc analysis (3% SE 30, 5' x ¼", 162°C) revealed approximately 77% of the starting material remaining and a 6% yield of ethyl phenylacetate.

Attempted Preparation of 1,3-Dicyanobutane. A 200-ml, 3-neck round bottom flask was fitted with an internal thermometer, a condenser topped by a vacuum adaptor, and a glass-ground stopper. Into the flask were placed 9.76 g (0.054 mole) of ethyl-2,4-dicyanopentanoate, 6.21 g (0.083 mole) of dried, powdered potassium chloride, 0.64 g (0.0025 mole) of 18-crown-6, and 35 ml of acetonitrile. A gas trap filled with saturated aqueous barium hydroxide solution was attached to the vacuum adaptor, and the solution refluxed for 16 hr. Negligible insoluble barium carbonate (the product formed between evolved carbon dioxide and barium hydroxide) formed in the gas trap during the reflux period. The procedure was repeated with xylene-benzene (7 hr at reflux), but with the same negative results.

Kinetic Studies with "Naked" Cyanide

Kinetics of 1-Chlorohexane

The constant-temperature water bath was equilibrated over a period of several days to 49°C. Meanwhile, 1.1220 g (0.004245 mole) of 18-crown-6 were weighed into a 25-ml volumetric flask, and the volume diluted to the mark with acetonitrile to give a 0.1698 M solution. The crown solution was placed over 1.70 g (0.026 mole) of dry, powdered potassium cyanide, and the mixture stirred vigorously for 1.5 hr with a magnetic bar. The stirring bar was removed, the solid compacted by centrifugation, and 20.0 ml of the "naked" cyanide solution carefully drawn off via a calibrated pipette (suction bulb) and placed in a 50-ml volumetric flask (0.90 g of crown (0.0034 mole)). Into a 10-ml volumetric flask were placed 0.6353 g (0.005267 mole) of 1-chlorohexane (Aldrich), the volume diluted to the mark with acetonitrile, and the liquid mixed with the "naked" cyanide solution in the 50-ml volumetric flask to give a final concentration of 0.1756 M in reactant and 0.11 M in crown. The flask was sealed by a rubber septum and the septum wired securely to the flask neck to prevent evaporation. After shaking, 1.0μl was quickly withdrawn into a syringe by use of a long needle inserted through the septum, the aliquot analyzed by glc (3% SE 30, 5' x ¼", 75°C), and the flask submerged in the 49°C constant temperature bath. Glc analysis revealed that the sample tested at room

temperature contained no 1-cyanohexane, and thus the time of immersion was designated as t_o. Aliquots after submersion were withdrawn at times t_1, t_2, t_3 . . . t_n . . . t_{end}, and the decrease in the area of the 1-chlorohexane peak (t_{ret} 1.4 min) and the increase in the area of the 1-cyanohexane peak (t_{ret} 2.0 min) was monitored by glc until no further change in the areas could be detected. After a short period of time from mixing, white particles of salt began to precipitate and the amount visually increased during the course of the reaction.

The equation used to analyze the data was the classical expression for second-order kinetics:

$$k\ (a_o - b_o)\ t = \ln \left[\frac{b_o\ (a_o - x_n)}{a_o\ (b_o - x_n)} \right]$$

where:

k = second-order rate constant

a_o= concentration of 1-chlorohexane at t_o (0.1756 M)

b_o= initial concentration of "naked" cyanide ion, x_{end}

t = time of reaction

x_n= difference between the concentration of 1-chlorohexane at t_o and at t_n , $a_o - a_n$

It had been demonstrated (see the synthesis of 1-cyanohexane, Method I) that 1-cyanohexane was the only product formed in the reaction between "naked" cyanide and 1-chlorohexane, and

it was assumed that the conversion was quantitative with respect to cyanide ion concentration and that the thermal conductivities (and hence the glc signal response factors[474]) of 1-chlorohexane and 1-cyanohexane were approximately equal. For each reaction aliquot tested by glc, the areas of the reactant and product peaks were carefully measured with a planimeter (5 to 10 measurements taken per aliquot and the average area computed). Using the stated observations and assumptions and the total area of the 2 peaks, the percentage of 1-chlorohexane remaining and the percentage of 1-cyanohexane having been formed at each t_n was calculated. As the initial concentration of 1-chlorohexane was known, a_o, and the percentage remaining at t_n calculated, computation of the concentration at t_n, a_n, (and hence the quantity x_n) followed in a straightforward manner. The initial concentration of "naked" cyanide ion, b_o, was found by essentially working "backwards". The value of x_{end} at t_{end}, i.e., the value after reaction was complete, was used as the value for b_o. In other words, by the stated observations and assumptions, the total moles of 1-chlorohexane converted to product was necessarily equal to the moles of anion present in the starting mixture. For this run, the value of b_o was determined to be 0.0693 M (0.00208 mole, 61% of the available crown complexed).

After the values of a_o, b_o, and x_n (for each t_n) were finalized, it remained to insert them into the second-order

kinetics equation and to plot t vs. ln $b_o (a_o - x_n) / a_o (b_o - x_n)$. A true second-order reaction gives a straight line for such a plot, with a slope of $k (a_o - b_o)$. The experimental data points, when visually plotted on common graph paper, approximated closely a straight line with a slope of 0.176. Inserting the known value of a_o and the derived value of b_o in the slope term, a second-order rate constant of 4.6×10^{-4} liter/mole-sec was obtained.

For a more accurate assessment of the data, a Wang 700 Series Advanced Programming Calculator-Computer was utilized. By the computer method, a slope of 0.183 and a k of 4.8×10^{-4} liter/mole-sec were obtained. On an accuracy scale of 0-1.0, the best straight line for the data was assigned for accuracy rating of 0.98 by the computer program.

Attempted Kinetics of 1-Bromohexane

The apparatus and procedure were the same as for the 1-chlorohexane kinetic run. Initial concentrations were 0.2502 M (0.007506 mole) in 1-bromohexane (Eastman) and 0.11 M (0.0034 mole) in 18-crown-6. After mixing the 1-bromohexane and "naked" cyanide solutions at room temperature and analyzing the mixture by glc (3% SE 30, 5' x ¼", 80°C) as quickly as possible (2-3 min from time of mixing until time of injection), it was discovered that substantial reaction had already occurred, and that white particles of salt were visible in the solution. The mixture consisted at this point of 76% 1-bromohexane and 24% of 1-cyanohexane (63% of reaction completed). The reaction was finished in 0.2 - 0.4 hr at 49°C, and the initial

concentration of "naked" cyanide, b_o, found to be 0.0968 M (0.00290 mole, 86% of the available crown complexed).

The reaction was thus extremely rapid, even at room temperature, for the homogeneous system (compare with the synthesis of 1-cyanohexane, Method II). Due to the fast rate of reaction and the physical limitations of the monitoring method being used, no accurate kinetics could thus be determined for the 1-bromohexane - "naked" cyanide reaction.

Attempted Kinetics of Benzyl Chloride

The apparatus and procedure was the same as for the 1-chlorohexane kinetic run. Initial concentrations were 1.009 M in benzyl chloride and 0.20 M in 18-crown-6. Immediately upon mixing the crown and "naked" cyanide solutions at room temperature, a fine white salt began to precipitate. Rapid glc analysis (2-3 min after mixing, 3% SE 30, 5' x ¼", 119°C) was conducted, and the reaction (kept at room temperature) monitored periodically for 9½ hr. The analysis revealed no change in the areas of the product and benzyl chloride peaks from the time of initial testing until the final aliquot was withdrawn, i.e., the reaction was completed almost instantaneously upon mixing. By utilizing the semi-quantitative half-band width method for measuring the peak areas and the observations and assumptions stated in the 1-chlorohexane kinetic run, it was calculated that approximately 29% of the mixture was benzyl cyanide. Due to the rapid rate of reaction and the physical limitations of the monitoring method, no accurate kinetics could thus be determined for the benzyl chloride - "naked" cyanide reaction.

CHAPTER VIII

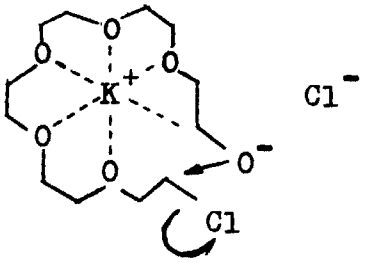
RESULTS AND DISCUSSION, CROWN ETHERS

Syntheses of Crown Ethers

1,4,7,10,13,16-Hexaoxacyclooctadecane (18-Crown-6)

As noted in the Introduction and Experimental sections, the majority of the work on the synthesis and purification of 18-crown-6 was accomplished by G. W. Gokel and H. P. Harris[105-109]. The contribution of the present author was thus limited to assistance in improving and perfecting the new procedure[108-109].

The flow diagram for the synthesis and purification is shown in Figure 11[105-109]. The main advantages of the novel procedure over earlier methods were the use of commercially-available substrates, wet reaction conditions, and simplicity (both in reaction procedure and work-up)[5,17,101-103]. The overall yield of cyclic product was comparable to that of Green[14,103] and Dale and Kristiansen[101-102], and superior to that of Pedersen[5]. The relatively high yield was due to the "template effect" of the potassium cation that facilitated closing of the ring, 11:



11

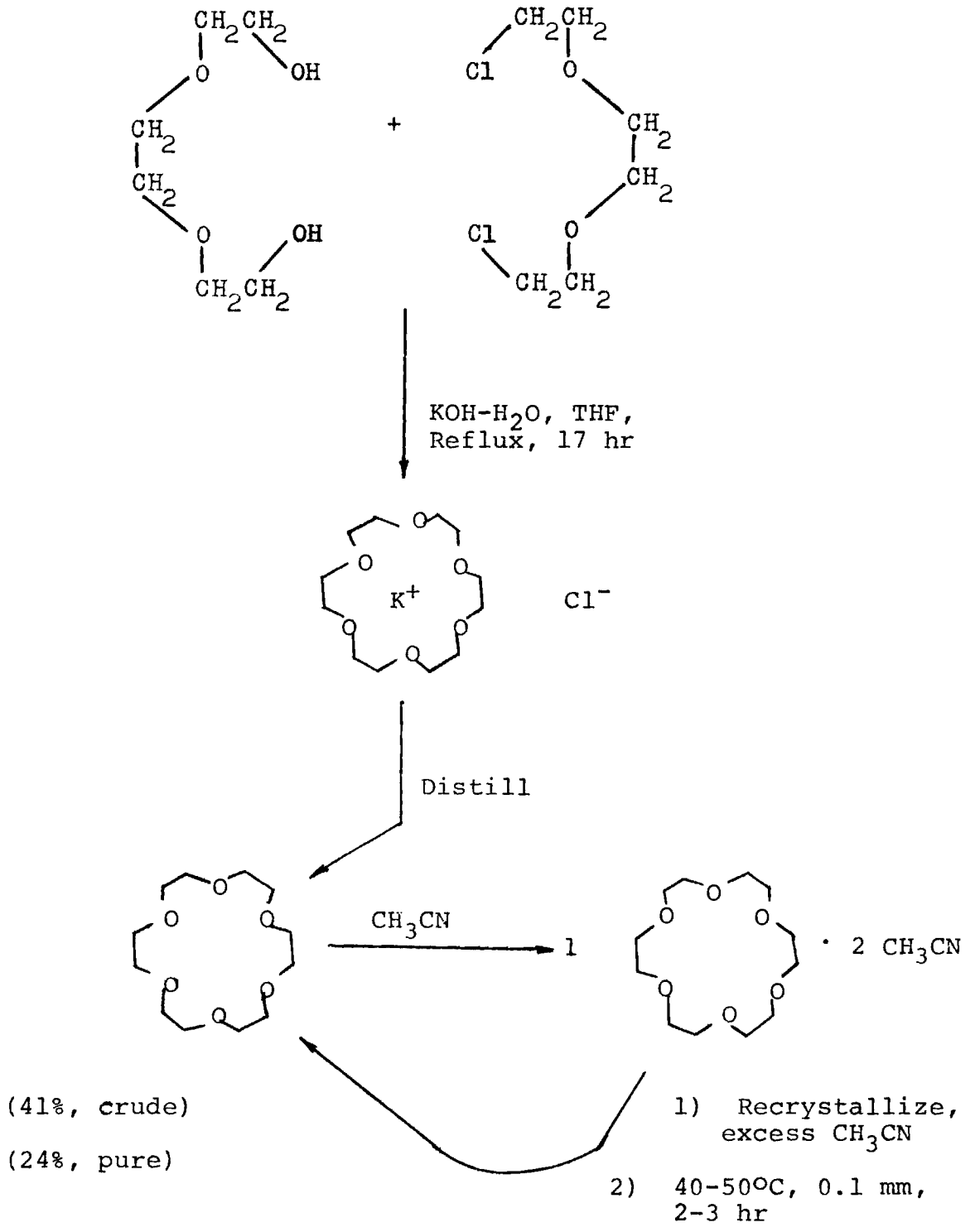


Figure 11. Flow Diagram for the Synthesis and Purification of 18-Crown-6.

The main impurities in the product mixture were hydroxyl-containing components, presumably linear polyethers. Distillation of the crown presented an extremely wide boiling range. DTA/TGA studies of the pure 18-crown-6 contained herein demonstrated that the thermal stability of the compound was low in the distillation temperature range, and hence fragmentation during volatilization despite high vacuum contributed to the impurities and expense of the range.

The purification procedure was unique in that a non-metallic crown complex was used to selectively separate the cyclic product from the linear comonents of the product mixture, followed by recrystallization in an excess of the complexing agent (CH_3CN) to further purify the product, and subsequent removal of the CH_3CN under vacuum[106]. The nature of the crown-acetonitrile complex has been elucidated (see the sections on crown-nitrile complexes). The yield of 18-crown-6 was improved by cooling the mother liquor of the recrystallization in ice-acetone, as a threshold must be passed in crown concentration before rapid complex formation proceeds at room temperature (ca. 0.2 M)[106]. Greater purity of the final product was obtained by collecting the distillate in several fractions instead of as a single portion, recrystallizing each fraction separately, and repeating the purification procedure several times to completely remove the hydroxyl-substituted impurities. The lower melting point of the isolated solid than that reported for 18-crown-6 indicated that the purification

techniques utilized by Greene had resulted in product contaminated with the higher-melting crown-potassium tert-butoxide complex[14]. Also, the liquid-to-solid distillation reported by Greene[14] was not easily repeated[106].

The violent behavior observed when the KOH solution was added to systems containing redistilled THF was unexplained. Due to the rapid coloration and rise in viscosity of the solution, some type of polymerization involving either THF or co-distilled olefins formed in the previous run may have been responsible. The commercial-grade solvent contained appreciable quantities of water, which possibly exerted a diluent effect on the exothermic process in the initial reactions.

1,4,7,10-Tetraoxacyclododecane (12-Crown-4)

Although Dale and coworkers have published a synthesis of 12-crown-4 by acid-catalyzed ethylene oxide tetramerization in yields comparable to those contained herein (15%), the procedure was hampered by its uncontrolled nature, i.e., a highly complex mixture of cyclic oligomers was obtained[119]. In addition, the reported 15% yield was by glc analysis, not being an isolated product figure[119].

Many combinations of reactants, solvents, and conditions were attempted before the accepted method for producing 12-crown-4 was obtained (Appendix 1). Due to the relative sizes of the "hole" of 12-crown-4 and the lithium cation, the latter was required in the system in order to provide the proper template effect[5,14-15]. Lithium bases (tert-butoxide and hydrated

hydroxide), however, were not successfully employed (Appendix 1). Since anhydrous lithium perchlorate had been found to offer a beneficial template effect in the acid-catalyzed tetramerization of furan and acetone (16-membered ring)[125-126]. the salt was employed with NaOH as the required base. The sodium cation was apparently too large to effect cyclization alone (Appendix 1). Another advantage of lithium perchlorate surfaced during work-up development, as the salt had been shown to be insoluble (no detectable solubility) in chlorinated hydrocarbons[475], and the explosive compound was thus separable from the complex by extraction of the aqueous solution with chloroform. DMSO was selected as the reaction solvent, as lithium salts (especially those with large anions) are exceptionally soluble in dipolar, aprotic solvents[476]. In addition, cations are much more solvated in DMSO than anions[476], and thus the possibility of an enhanced template effect due to more efficient solvent-separated ion pairs existed. Although the solvating ability of DMSO had been attributed to interaction of the cation with the region of high electron density localized on the bare oxygen atom of the solvent[477], results with 18-crown-6-potassium tert-butoxide in DMSO had indicated that the crown satisfied completely the coordination sites of the cation even to the exclusion of the solvent[230].

The flow diagram for the developed synthesis of 12-crown-4 is located in Figure 12. The physical properties were consistent with those reported for the compound prepared

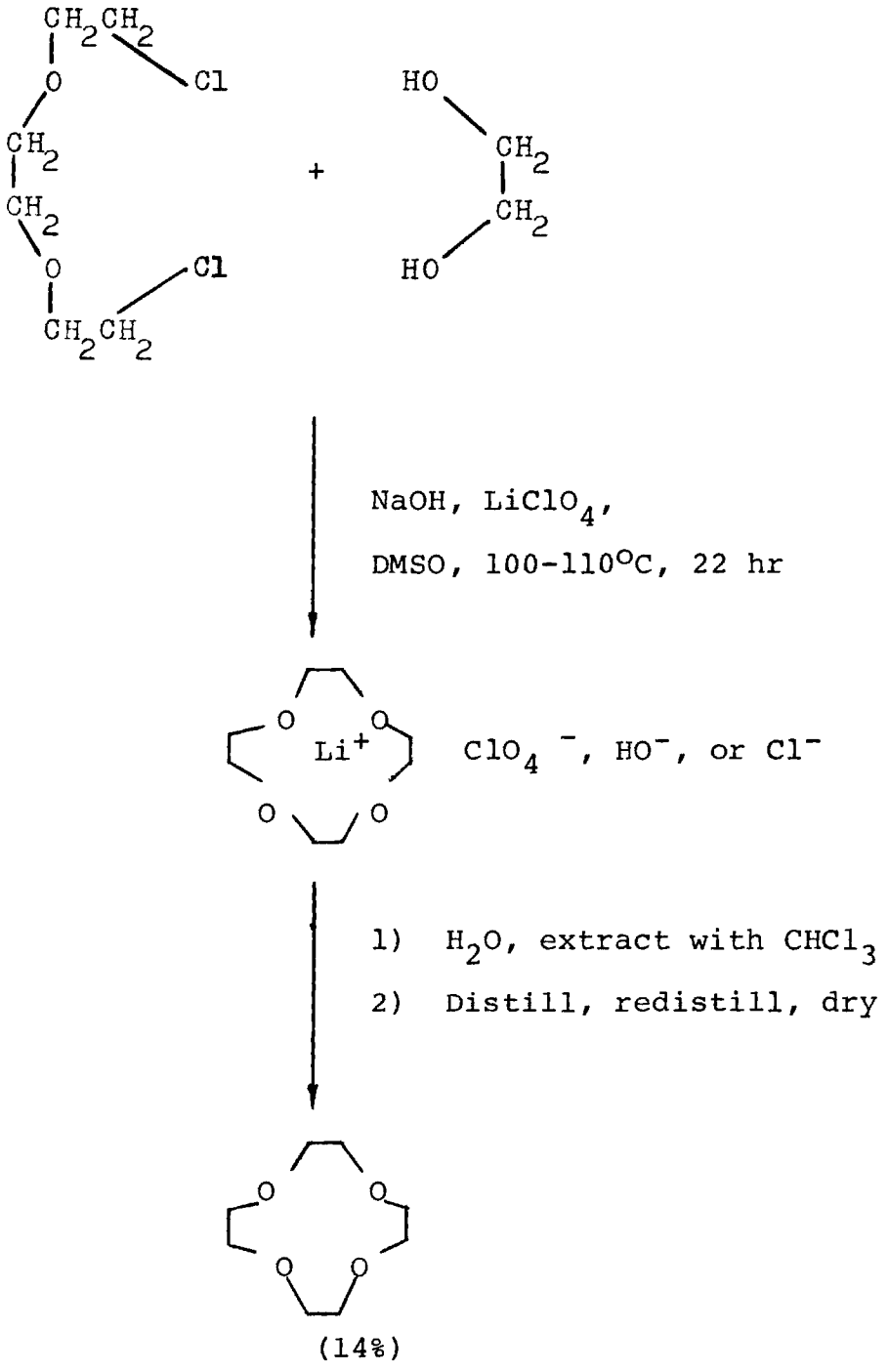


Figure 12. Flow Diagram of the Developed Synthesis of 12-Crown-4.

by tetramerization of ethylene oxide[113,118-121]. The yield was comparable to the older method, but separation of cyclic product mixtures was avoided[119]. No vigorous attempt was made to optimize the yield. In contrast to the 18-crown-6 synthesis, no H_2O was added to the commercial-grade solvent to enhance base solubility, as the runs with hydrated LiOH had indicated that the lithium cation was too strongly solvated by the water to effectively act as a template. The exothermic reaction observed on adding the anyhydrous $LiClO_4$ to the DMSO-NaOH system was due either to released energy of solvation of the perchlorate salt or an exchange reaction between the $LiClO_4$ and NaOH:

$$LiClO_4 + NaOH \longrightarrow NaClO_4 + LiOH$$

Thus the possibility existed that the active reagent in the condensation-cyclization process was nonhydrated LiOH formed in situ.

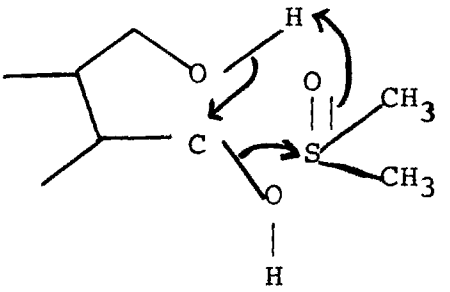
Although undesirable due to an ability to partition between solvents, solubilization of the 12-crown-4 reaction mixture in water followed by extraction was necessary, as attempted distillation of other $LiClO_4$-containing systems in which the salt was not completely removed resulted in minor explosions. The solution in water resulted in a tenacious complex or hydrate of the 12-crown-4 and H_2O. The affinity for water was not unexpected in view of the crystalline 2:1 (crown:salt) pentahydrate complex with sodium chloride

isolated by van Remaartere and Boer[117] and the reported formation of clathrate hydrates of ethylene oxide and 1-methyl-1,3-dioxane[220]. By ir analysis, the H_2O was reduced drastically by stirring the isolated material over molecular sieves.

The ir spectra, taken with NaCl plates, gave sharp bands in the 1200-1000 cm^{-1} region. As shown by Dale and coworkers[120], these bands were sharpened considerably in the LiBr-crown complex (1:1) in comparison to the spectra of uncomplexed 12-crown-4 (polyethylene film), and thus complexation of the crown with the NaCl plates utilized in the present study was probable.

The presented synthesis of 12-crown-4 has been published[131]. Literature reviews of the procedure have been favorable[478].

Several unsuccessful attempts were made to cyclize tetraethylene glycol directly to 12-crown-4 in DMSO alone or with added $LiClO_4$ at high temperatures (Appendix 1). The attempts were based on literature reports that 1,4-diols dehydrated in DMSO at greater than 150°C <u>via</u> the transition state <u>12</u> to give furan derivatives in good yields[479-480]:



<u>12</u>

1,4,8,11-Tetraoxacyclotetradecane (14-Crown-4)

As no combinations of glycol ethers and dichloride ethers to produce 14-crown-4 were commercially available, the developed 12-crown-4 reaction system was used with 1,3-dichloropropane and ethylene glycol in hopes of cyclizing 2 monoadducts formed in situ. Although nmr spectra of the crude product indicated that 14-crown-4 had been formed, the yield was so low (0.6%, crude) that the procedure was not considered practical as a general synthetic route.

Complexes of 18-Crown-6 with Nitrile Compounds

Syntheses of Crown-Nitrile Complexes

Relatively few non-metallic crown complexes have been reported in the literature[133-134,215-223]. After discovery of the crystalline 18-crown-6-acetonitrile complex used in the purification of the cyclic polyether[106], interest developed in characterizing the initial complex and exploring the generality of the phenomenon with other nitril compounds.

A series of 18-crown-6-nitrile complexes were thus synthesized and their properties determined. A summary of the complexes produced (including recrystallized complexes) and their melting points and nmr stoichiometries is contained in Table 6. The succinonitrile and malononitrile complexes were synthesized, partially characterized (^{1}H- and ^{13}C-nmr, ir, mp), and supplied by R. T. Henson[236], and are included in this work for completeness. Elemental analyses for selected complexes are detailed in Table 7. Several of the complexes were easily

Table 6. Melting Points and ^{1}H-NMR Analyses of 18-Crown-6-Nitrile Complexes.

Nitrile Compound	Recrystal. Solvent	Melt Pt. (°C)	Normalized NMR Integration (Crown:Nitrile)	H-Ratio Calc.[1]	Stoichiometry by NMR (Crown:Nitrile)
Acetonitrile (fine)	-	63.5-65.5	4.96:1	5.33:1	2:3[2]
Acetonitrile (fine)	CCl_4	62.5-65.5	5.73:1	5.33:1	2:3[2]
Acetonitrile (plate)	-	72-75	4.06:1	4.00:1	1:2
Acetonitrile (plate)	CCl_4	70-72	4.21:1	4.00:1	1:2
Acrylonitrile	-	34.5-35.5	5.53:1	5.34:1	2:3
Glutaronitrile	-	47-48	1.75:1	2.00:1	1:2
Glutaronitrile	CCl_4	47.5-48	2.00:1	2.00:1	1:2
Adiponitrile	-	50-52	2.87:1	3.00:1	1:1
Adiponitrile	CCl_4	51-52	2.12:1	2.00:1	2:3
Adiponitrile	C_6H_6	51-52	2.55:1	-	Uncertain[3]
δ-Chlorovalero-nitrile	-	36.5-38	2.98:1	3.00:1	1:1

Table 6. Melting Points and ^{1}H-NMR Analyses of 18-Crown-6-Nitrile Complexes (Continued).

Nitrile Compound	Recrystal. Solvent	Melt Pt. (°C)	Normalized NMR Integration (Crown:Nitrile)	H-Ratio Calc.[1]	Stoichiometry by NMR (Crown:Nitrile)
1,2-Dicyano-propane	-	69-70.5	1.74:1	2.00:1	1:2
1,2-Dicyano-propane	CCl_4	70-70.5	1.79:1	2.00:1	1:2
Succinonitrile[4]	CCl_4	83-84	2.50:1	3.00:1	1:2
Malononitrile[4]	C_6H_6	127-129	5.80:1	6.00:1	1:2

[1]Calculated values based on the assigned stoichiometries, which in turn possessed hydrogen ratios nearest to the nmr values for the possible integral complexes.
[2]The 2:3 stoichiometry was found by elemental analyses to be erroneous (Table 7), with the actual stoichiometry being 1:2
[3]The experimental H-ratio was midway between the calculated values for a 2:3 and a 1:1 complex (2.00:1 and 3.00:1, respectfully), and thus the actual stoichiometry was uncertain.
[4]Synthesized, partially characterized, and supplied by T. R. Henson[236].

Table 7. Elemental Analyses of Selected 18-Crown-6-Nitrile Complexes.

Nitrile Compound	Recryst. Solvent	Elemental Analyses Found C	Found H	Found N	Calculated[1] C	Calculated[1] H	Calculated[1] N	Stoichiometry by EA (Crown:Nitrile)
Acetonitrile (fine)	-	55.44	8.72	7.98	55.47	8.73	8.09	1:2
Acetonitrile (plate)	-	55.37	8.78	7.98	55.47	8.73	8.09	1:2
Acrylonitrile	-	57.52	8.34	6.16	57.62	8.35	6.11	2:3
Glutaronitrile	CCl_4	58.26	8.05	12.30	58.38	8.02	12.38	1:2
Adiponitrile	C_6H_6	61.35	8.73	7.18	58.04[2]	8.66	7.52	Uncertain[2,3]
					59.13[3]	8.51	9.85	
δ-Chlorovalero-nitrile	-	53.21	8.20	4.18	53.46	8.45	3.67	1:1
1,2-Dicyano-propane	CCl_4	58.69	7.89	12.57	58.38	8.02	12.38	1:2
Succinonitrile[4]	CCl_4	57.06	7.68	13.28	56.58	7.60	13.20	1:2
Malononitrile[4]	C_6H_6	54.47	7.14	14.16	54.53	7.12	14.14	1:2

[1]The calculated elemental analysis is for the assigned stoichiometry.
[2]Calculated values for a 1:1 crown:adiponitrile complex.
[3]Calculated values for a 2:3 crown:adiponitrile complex.
[4]Synthesized, partially characterized, and supplied by T. R. Henson[236].

recrystallized in non-polar solvents, itself an interesting phenomenon accentuating the strength of attraction between the components. A wide range of stoichiometries and melting points were exhibited, with the physical constants dependent on the nitrile precursor employed. With the exception of the acrylonitrile-crown complex, all of the novel compounds melted at or considerably higher than pure 18-crown-6 (36.5-38^{o}C). In addition, the exceptionally stable succionitrile- and malononitrile-crown complexes melted higher than the solid nitrile precursors (57.2^{o}C and 32^{o}C, respectively)[236]. The variation in molecular ratios, melting points, and physical forms of the various complexes indicated the unpredictable nature of the compounds. Although no definite interpretation could be placed on the data shown in Figure 13 due to the small number of points graphed, the relationship obtained by plotting melting point *vs.* number of methylene units in the series $NC(CH_2)_nCN$, n=1, 2, 3, 4, in conjunction with the determined stoichiometries for these complexes was interesting. The melting points for the first 3 members of the series decreased *ca.* 40^{o}C for each methylene unit added to the carbon skeleton, and each of the 3 possessed a 1:2 stoichiometry (crown:nitrile). Adiponitrile (n=4) did not follow the general pattern, however, melting higher than glutaronitrile and exhibiting a complicated stoichiometry.

The acetonitrile complex formed in 2 distinct physical forms. Vigorous stirring of the hot, saturated solution

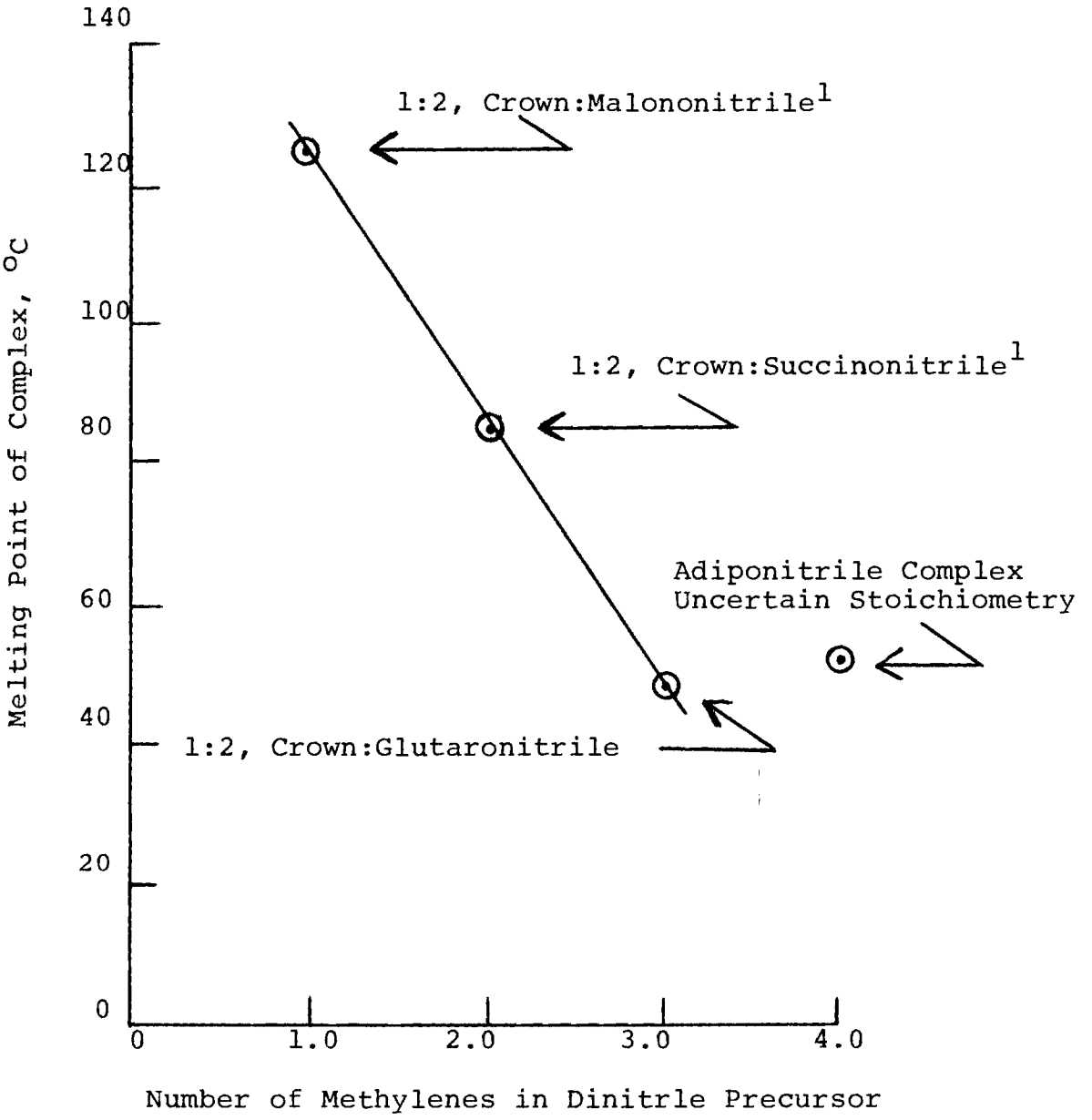


Figure 13. Relationship between the Melting Points of 18-Crown-6-Dinitrile Complexes, the Number of Methylene Units in the Dinitriles, and the Stoichiometries of the Complexes.

[1]Synthesized, partially characterized, and supplied by T. R. Henson.[236]

of crown in CH_3CN produced fine white crystals, while stacked, transparent platelets formed if the solution was allowed to cool undisturbed. Although nmr analyses indicated that the stoichiometries of the 2 physical forms were different (Table 6), elemental analyses confirmed that both were of the same molecular ratio (Table 7). The error was caused by the difficulty encountered in analyzing accurately the nmr integration of the CH_3CN-crown complexes due to the large differences between the number of hydrogens of the components. Elemental analyses of the remaining complexes confirmed the stoichiometries determined by nmr.

The adiponitrile complexes were not as well-defined as the others examined. From consideration of the nmr results for the initial complex and those obtained on recrystallization from CCl_4 and C_6H_6, it appeared that all 3 had different molecular ratios. Elemental analysis of the C_6H_6-recrystallized complex, however, signified that the stoichiometries were complicated, i.e., non-integer in character. The position of the adiponitrile-crown complex in Figure 13 tempted speculation that a new crystalline arrangement, forced either by increasing bulk or length or a combination of factors, had formed on progressing from glutaronitrile to adiponitrile. The amount of data, however, was insufficient to draw a definite correlation.

The sterically-hindered complex of benzonitrile and crown was unstable, melting at ca. 0°C. The phenyl group

was apparently too bulky to effectively lock into a stable crystal structure containing the macrocyclic rings of 18-crown-6.

In view of the stoichiometries obtained, it appeared unlikely that the linear -C≡N group was inserted directly into the "hole" of the crown, as Gokel and Cram have theorized for the corresponding (but positively charged) functional groups of arenediazonium and arylacylonium salts[215]. The low molecular ratios, however, and the consistency between the stoichiometries of the initial and recrystallized complexes dictated that clathrate-type inclusion complexes were not formed[218].

DTA/TGA, IR, and ^{13}C-NMR Analyses of Crown-Nitrile Complexes

Questions arose as to whether the crystalline crown-nitrile solids were actually true complexes[108]. With the exception of metal ion-crown complexes where crystalline structures have been determined, the nature of the interactions between the host macrocyclic polyether and the guest molecule were not clearly understood[218]. The possibility existed that different substrates interact differently with the host, forming 1 case a complex, in another a solvate, et. The large size of the flexible ring may have trapped the molecules interstitially to gain a more favorable crystal lattice, while the multiple electronegative heteroatoms in the ring possessed the potential for interacting with and further ordering the guest molecule in the lattice. The term

"complex" between organic molecules has been defined as "a substance formed by the interaction of 2 or more component molecules (and/or ions) which may have an independent crystal structure and which will reversibly dissociate into its components, at least partially, in the vapor phase and on dissolution."[481] Such complexes are formed by weak interaction of electron donors with electron acceptors[481]. Thus DTA/TGA, ir, and ^{13}C-nmr analyses of the crystalline crown-nitrile solids were conducted in an attempt to decipher whether or not the materials were true complexes.

The results of the DTA/TGA studies for the selected adducts up to the melting points are located in Table 8. The endotherms associated with melting of the complexes peaked at temperatures comparable with the melting points obtained by visual means (Table 6). No transitions, either endothermic or exothermic, were observed for any of the DTA curves below the melting endotherm. The acetonitrile and acrylonitrile complexes had been observed to lose weight while sitting at room temperature during the elemental analyses. Accordingly, the TGA showed a moderate loss of weight for the 18-crown-6-CH_3CN complexes to the peak of the melting endotherm. No melting endotherm was observed for the unstable acrylonitrile-crown complex (Table 6). The adducts with low-boiling nitriles, however, were considered weak complexes by the stated definition[281], however, as no DTA transitions were observed below the melting points. As the DTA/TGA of pure 18-crown-6 demonstrated that the compound was thermally

Table 8. DTA/TGA Results for Selected 18-Crown-6-Nitrile Complexes.

Nitrile Compound	Recryst. Solvent	Melting Endotherm (peak, °C)	Wt. Loss at Endotherm (peak, %)
Acetonitrile (fine)	-	60	10.5
Acetonitrile (plate)	-	68	14.4
Glutaronitrile	-	50	Negligible
Adiponitrile	C_6H_6	53	Negligible
Succinonitrile[1]	CCl_4	87	Negligible
Malononitrile[1]	C_6H_6	130	2.7
1,2-Dicyano-propane	CCl_4	71	Negligible
δ-Chlorovalero-Nitrile	-	40	Negligible

[1]Synthesized, partially characterized, and supplied by T. R. Henson[236].

degrading above 120°C, the small (2.7%) weight loss observed for the malononitrile-crown complex at the relatively high mp was considered insignificant.

The low thermal stability of the pure 18-crown-6 explained the difficulties encountered on distilling the compound (see the previous section). The unstable behavior also emphasized the inadequacy of the isolation procedure for the crude crown[105-109].

Routine ir analyses indicated a shift of the nitrile stretch absorption in the region 2200-2250 cm^{-1} to slightly lower wavenumbers on complexation. High-resolution ir analyses (accurate to $\pm$ 0.2 cm^{-1})[482] of the critical region confirmed the indication, as shown in Table 9. The shifts were small but discernible, and all followed the same general pattern (to lower wavenumbers). As a decrease in stretching frequency indicated a decrease in bond strength[483], apparently the nitrile triple bond was weakened on complexation. Hence the ir absorptions were shifted in the intuitively-correct direction for the bond's postulated role as an electron acceptor within the classical definition of a complex[481]. With the exception of the weak acrylonitrile-crown complex, the magnitude of the shift followed the melting point order of the complexes, i.e., the higher the mp, the greater the shift.

Fedarko has reported slight movement to lower chemical shifts of the methylene carbon absorptions of dicyclohexyl-18-crown-6 and dibenzo-18-crown-6 when complexation with potassium cation was effected in CD_2Cl_2[185]. The results obtained by ^{13}C-nmr for the presented crown-nitrile complexes in solution are shown in Table 10. Although the changes in chemical shift for the crown methylenes upon complexation were somewhat less than those observed by Fedarko, the direction of change (to lower ppm) was the same in all cases, and thus followed the general pattern reported[185]. The smaller

Table 9. High-Resolution Infrared Analyses of Selected 18-Crown-6-Nitrile Complexes.

Nitrile Compound	Recryst. Solvent	C≡N Position[1] Pure (cm^{-1})	Complex (cm^{-1})	Shift[2] (cm^{-1})
Acetonitrile (fine)	-	2237	2237	3
Acrylonitrile	-	2215	2207	8
Glutaronitrile	-	2235	2231	4
Adiponitrile	CCl_4	2231	2227	4
Succinonitrile[3]	CCl_4	2226	2221	5
Malononitrile[3]	C_6H_6	2251	2242	9

[1]The 1601 cm^{-1} peak of styrene was used as a standard.
[2]Calculated as the position of the pure nitrile compound minus the nitrile position in the complex.
[3]Synthesized, partially characterized, and supplied by T. R. Henson[236].

changes were reasonable, as the effect of the weak charge-transfer complexation with the nitriles on the crown methylenes would not be expected to be as great as with the fully-ionized potassium ion-crown complexes of Fedarko[185]. In addition, the effect on the spectra of using unsubstituted 18-crown-6 in the present study instead of the substituted derivatives[185] was undetermined. The direction of change for the nitrile carbon chemical shift varied with the nitrile precursor employed, and the magnitude of change was greatest for the complexes that also exhibited the highest melting points (Tables 6 and 10).

Table 10. ^{13}C-NMR Analyses of Selected 18-Crown-6-Nitrile Complexes.

Nitrile Compound	Recryst. Solvent	NMR Solv.	Chem. Shifts[1] Precursors Crown (ppm)	Chem. Shifts[1] Precursors C≡N (ppm)	Chem. Shifts[1] Complexes Crown (ppm)	Chem. Shifts[1] Complexes C≡N (ppm)	Change in Shifts[2] Crown (ppm)	Change in Shifts[2] C≡N (ppm)
Acetonitrile (plate)	-	$CDCl_3$	70.742	116.915	70.681	117.158	0.061	-0.243
Acrylonitrile	-	$CDCl_3$	70.742	117.037	70.681	116.915	0.061	0.122
Glutaronitrile	-	$CDCl_3$	70.742	118.430	70.560	118.308	0.182	0.122
Adiponitrile	CCl_4	$CDCl_3$	70.742	119.279	70.560	119.100	0.182	0.179
Succinonitrile[3]	CCl_4	$CDCl_3$	70.742	117.459	70.713	118.129	0.029	-0.670
Malononitrile[3]	C_6H_6	$CD_3\overset{O}{C}CD_3$	71.106	112.547	70.742	113.275	0.464	-0.728
Malononitrile[3]	C_6H_6	CD_3CN	71.167	111.698[4]	70.985	112.790[4]	0.182	-1.092

[1]Chemical shifts are in ppm from tetramethylsilane (TMS) as an internal standard.
[2]Calculated as the chemical shift of the pure precursor functionality ($^{13}CH_2$ of the crown and $^{13}C\equiv N$ of the nitrile) minus the chemical shift of the corresponding functionality in the solution of the complex.
[3]Synthesized, partially characterized, and supplied by T. R. Henson[236].
[4]The values given are for the malononitrile $^{13}C\equiv N$, not the nitrile functionality of CD_3CN.

As shown in the comparative spectra of the malononitrile complex[236], the nature of the nmr solvent also influenced the magnitude (though not the direction) of the changes. The influence of the competing nitrile in CD_3CN as the nmr solvent was undetermined. Use of CD_3CN as a nmr solvent was possible due to the slight solubility of 18-crown-6 observed in the dipolar, aprotic solvent (ca. 0.2 M at 25°C[106]). The ^{13}C-nmr spectra indicated that the complexes were at least partially associated in the relatively polar solvents[481], though the effect of complexation on the changes in chemical shifts were too small to draw definite conclusions as to the degree of association.

In summary, the DTA/TGA, high-resolution ir, and ^{13}C-nmr results, in conjunction with the melting point data, all signified that the crystalline 18-crown-6-nitrile solids satisfied the accepted definition as complexes[481]. Although the data obtained characterized the complexes in a general sense, single-crystal X-ray analyses will be required to elucidate the actual structures[215,218]. Although attempted X-ray structural analysis of the CH_3CN-18-crown-6 complex (plate crystals) has not been successful to date, results obtained with the related 1:2 crown:cyanogen bromide complex[236] have supported the work contained herein[484]. The results obtained for the crown-nitrile complexes have been submitted for publication[224].

Reactions Utilizing "Naked" Cyanide

General Results

As shown in Tables 11-15, the displacement, elimination, and addition reactions performed with potassium cyanide solubilized in CH_3CN or C_6H_6 proceeded smoothly and mildly to high yields of products. The reactions were carried out by simply pouring a substrate-18-crown-6 solution directly over excess, dry KCN and stirring the 2-phase system vigorously at ambient or reflux temperature until conversion was complete. Little or no reaction was found to take place in the absence of crown under the same conditions covering the same periods of time. In all cases, 18-crown-6 was present in catalytic quantities, indicating that it behaved as a phase-transfer catalyst[286-291]. In general, the reactions were more rapid in CH_3CN than in C_6H_6, and the former was determined to be the preferred solvent. Isolated yields of representative samples supported the accuracy of the glc monitoring procedure (half-width band method[474], no internal standards). The half-life of the reaction ($t_{\frac{1}{2}}$, time required for 50% of the starting material to react) was found by plotting the percentage of starting material remaining (as determined glc and/or nmr) vs. time. An example of a monitoring graph (1,3-dibromopropane demonstrated) is exhibited in Figure 14. For comparative purposes, representative literature preparations of nitrile compounds are detailed in Appendices 2 and 3.

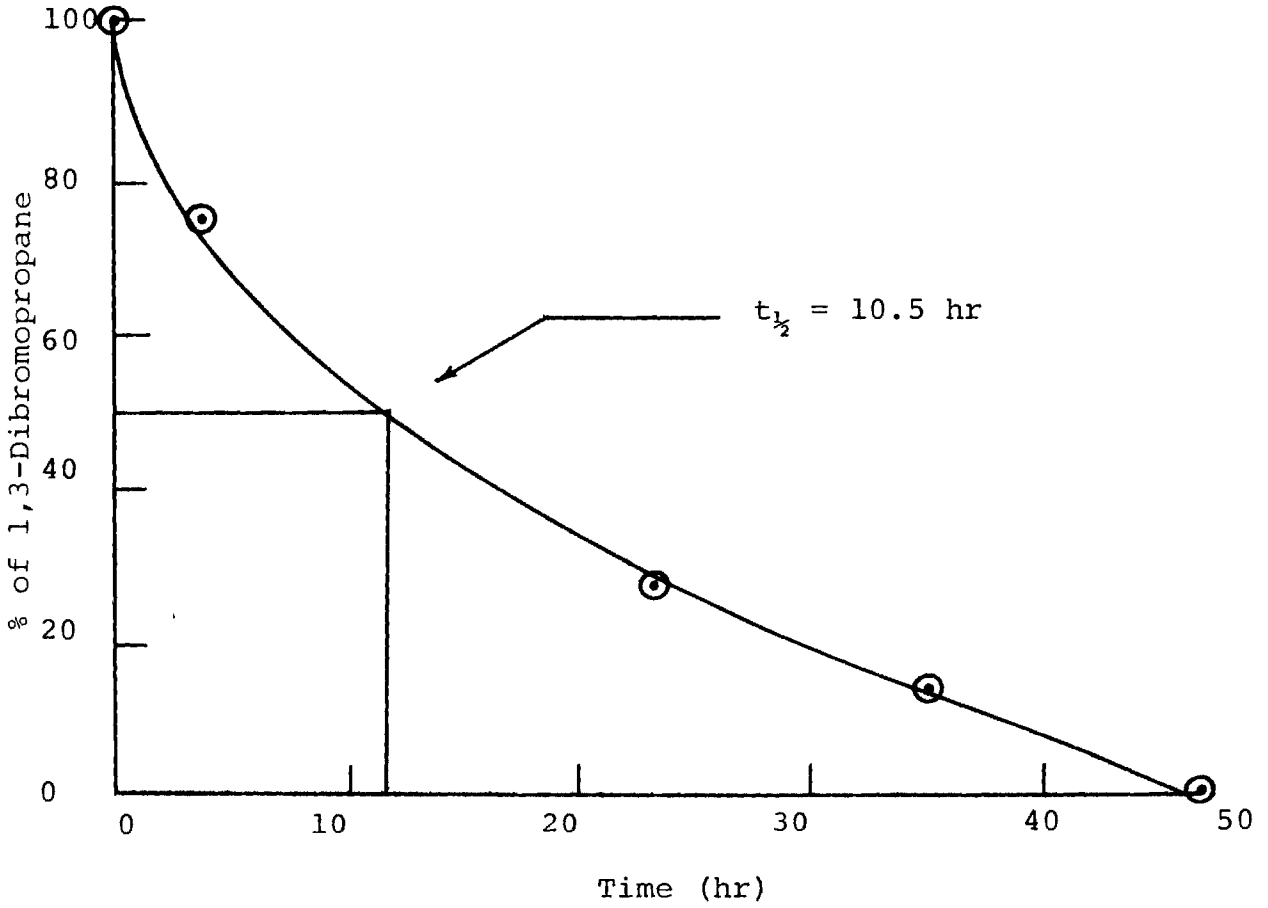


Figure 14. GLC Monitor Diagram for the Reaction of 1,3-Dibromopropane with "Naked" Cyanide in CH_3CN at Ambient Temperature.

Displacement and Elimination Reactions

The results of the displacement of primary halides by "naked" cyanide in the presence of 18-crown-6 are shown in Table 11. The displacements were quantitative by glc and nmr, with no elimination products detected. The reaction with benzyl chloride proceeded rapidly and quantitatively to product under mild conditions. As reported for the ethanol-water systems, 1,4-dichlorobutane reacted faster with "naked" cyanide than did 1,3-dichloropropane in comparative reactions (Table 11)[255,260,270].

Interestingly, primary chlorides were found to react much faster than the corresponding bromides under the reaction conditions. For example, benzyl chloride reacted over 100 times faster than benzyl bromide in a comparison of $t_{\frac{1}{2}}$. This observation was contrary to the normally-accepted leaving group order[485], and was also contrary to what had been reported for all but 1 of the other cyanide systems (Appendix 2). The lone exception was the work of Brandstrom, who found similar rate results as contained herein with cyanide ion in liquid poly(ethylene glycols)[268]. The reversal in reactivity was also contrary to what had been demonstrated with "naked" fluoride and "naked" acetate[106,253-254]. Dichlorides with 3 methylenes units in the chain reacted faster than those with 4 as expected[255], but contrary to the literature methods, the analogous dibromides reacted roughly at the same rate. Another curiosity was that the half-lives for the

Table 11. Total Displacement of Primary Halides by "Naked" Cyanide in the Presence of 18-Crown-6.

Substrate	Solv.	Concentration[1] Crown (M)	Substr. (M)	Temp.	Time $t_{1/2}$[2] (hr)	$t_{com.}$[2] (hr)	Product	Yield glc, nmr[3] (%)	Yield isolated[3] (%)
1-Chloro-hexane	CH_3CN	0.14	1.8	Reflux	0.2	2.2	1-Cyano-hexane	100	91
1-Bromo-hexane	CH_3CN	0.14	1.8	Reflux	10	40	1-Cyano-hexane	100	-
Benzyl Chloride	CH_3CN	0.14	2.1	Amb.	0.08	0.4	Benzyl Cyanide	100	94
Benzyl Chloride	CH_3CN	0.0	1.8	Amb.	-	75[4]	Benzyl Cyanide	20	-
Benzyl Bromide	CH_3CN	0.15	1.8	Amb.	13	25	Benzyl Cyanide	100	-
1,3-Dichloro-propane	CH_3CN	0.15	1.8	Reflux	0.2	1.5	1,3-Dicyano-propane	100	97[5]
	CH_3CN	0.15	1.8	Reflux	0.2	1.5			
1,3-Dichloro-propane	CH_3CN	0.15	1.8	Reflux	-	1.75	1,3-Dicyano-propane	100	92.5[5]

Table 11. Total Displacement of Primary Halides by "Naked" Cyanide in the Presence of 18-Crown-6 (Continued).

Substrate	Solv.	Concentration[1] Crown (M)	Concentration[1] Substr. (M)	Temp.	Time $t_{1/2}$[2] (hr)	Time $t_{com.}$[2] (hr)	Product	Yield glc, nmr[3] (%)	Yield isolated[3] (%)
1,3-Dibromo-propane	CH_3CN	0.15	1.8	Reflux	7	25	1,3-Dicyano-propane	100	97
1,3-Dibromo-propane	CH_3CN	0.15	1.8	Amb.	10.5	48	1,3-Dicyano-propane	100	97
1,3-Dibromo-propane	CH_3CN	0.15[6]	1.8	Reflux	-	25	1,3-Dicyano-propane	100	-
1,3-Dibromo-propane	C_6H_6	0.15	1.8	Amb.	10	46	1,3-Dicyano-propane	100	-
1,3-Dibromo-propane	C_6H_6	0.15	1.8	Reflux	12	40	1,3-Dicyano-propane	100	-
1-Bromo-3-Chloropropane	CH_3CN	0.15	1.8	Reflux	1	30	1,3-Dicyano-propane	100	-
1,4-Dichloro-butane	CH_3CN	0.14	1.8	Reflux	0.2	0.7	1,4-Dicyano-butane	100	95

Table 11. Total Displacement of Primary Halides by "Naked" Cyanide in the Presence of 18-Crown-6 (Continued).

Substrate	Solv.	Concentration[1] Crown (M)	Concentration[1] Substr. (M)	Temp.	Time $t_{1/2}$[2] (hr)	Time $t_{com.}$[2] (hr)	Product	Yield glc, nmr[3] (%)	Yield isolated[3] (%)
1,4-Dichloro-butane	CH_3CN	0.14	1.8	Amb.	8	75	1,4-Dicyano-butane	100	86
1,4-Dibromo-butane	CH_3CN	0.14	1.8	Reflux	6.5	14	1,4-Dicyano-butane	100	-
1,4-Dibromo-butane	CH_3CN	0.14	1.8	Amb.	11	57	1,4-Dicyano-butane	100	-

[1]The reactions were run in a total of 25 ml of solution, with a 2-fold excess of solid KCN per functional group converted.
[2]The time required for 50% of the starting material to react was defined as $t_{1/2}$, and $t_{completion}$ was the time required for complete formation of the final product.
[3]The half-width band method[474] was used to determine the glc yield, with isolated yields for representative cases instead of internal standards used to validate the accuracy of the glc procedure. Nmr spectra (where applicable) exhibited only peaks for the stated product.
[4]The reaction was halted before completion.
[5]The first run (97%) included continuous extraction in the work-up, while in the second run (92.5%) hand-extraction techniques were utilized.
[6]Catalytic KCl (0.019 moles) was used in conjunction with 0.18 moles of KCN.

1,3-dibromopropane and 1,4-dibromobutane reactions were comparable regardless of the reaction temperature, i.e., progression from ambient temperatures to reflux did not significantly influence $t_{½}$. The reflux temperatures, however, did lead to shorter times of completion. Benzyl bromide was observed to convert rapidly up to ca. 10% product by glc, but then the rate slowed drastically and remained slow for the remainder of the process. The reaction of 1-bromo-3-chloropropane with "naked" cyanide at reflux gave a $t_{½}$ which was slightly higher than that for 1,3-dichloropropane under comparable conditions, but which was far below that of 1,3-dibromopropane (1 hr vs. 15 hr, respectively). However, the $t_{completion}$ for the mixed dihalide was comparable to that of the dibromo reagent (30 hr vs. 25 hr, respectively), while using 20 times slower than for 1,3-dichloropropane (Table 11).

Brandstrom attributed the reversal in rate in the poly(ethylene glycol)-cyanide system to the heterogeneous character of the reaction, with relative solubilities of the salts considered important to the rate[268]. Since they Brandstrom paper appeared, polyglycol dimethyl ethers have been shown to form weak complexes with cations in solution[55], while crystalline complexes of poly(ethylene oxide) with several metal salts have been synthesized[57]. It was suspected, therefore, that the reason for the reactivity reversal both in the earlier work[268] and in the current investigation lay in the relative complexing abilities of linear or macrocyclic

polyethers for the salts involved in the reaction of cyanide ion with alkyl halides (KCN, KCl, and KBr).

A diagram of the suspected equilibria involved in the reactions with "naked" anions (cyanide ion pictured) is detailed in Figure 15. The lattice energy (the energy required to separate the ions of a crystal to an infinite distance from each other[486]) of potassium chloride is 6.1 kcal/gfw greater than that of potassium bromide[487]. A. Dabdoub, utilizing flame photometry, has determined molar solubilities of KCN, KBr, and KCl in 0.15 M 18-crown-6-CH_3CN solution at 25°C to be 1.29×10^{-1}, 1.35×10^{-1}, and 5.55×10^{-2}, respectively, with a relative order of solubilities as follows[488]:

$$KBr \approx KCN > > KCl$$

Apparently in the reaction sequency (Figure 15), the rate of deposition of KCl from solution to regenerate free (uncomplexed) crown is much faster than that for KBr, i.e., $k^3_{Cl} > > k^3_{Br}$. As the crown was present in catalytic quantities, the concentration of free crown available to complex with the KCN and thus bring more of the "naked" cyanide into solution was critical to the rate. As the solubilities of KCN and KBr were found to be similar in CH_3CN[488], k^1_{CN} and k^{-3}_{Br} should have been comparable, with $k^1_{CN} >> k^{-3}_{Cl}$.

The results thus are consistent with an increased tendency for KCl to precipitate readily out of solution to regenerate uncomplexed crown. For alkyl bromides, the KBr

tends to remain complexed in solution, and thus ties up the 18-crown-6 so that the rate of reaction is slowed for lack of cyanide ion (indicating an Sn2 process).

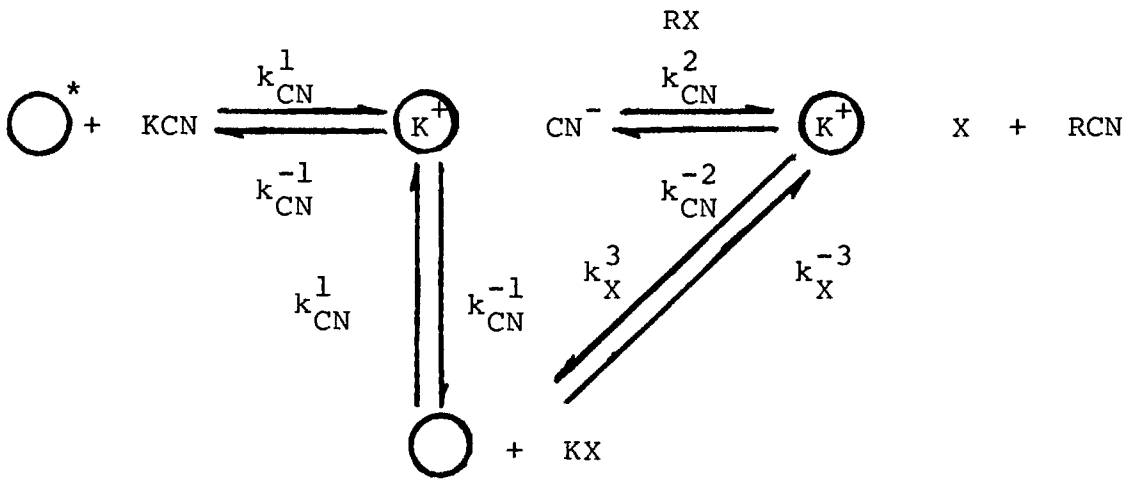


Figure 15. Equilibria Involved in the 18-Crown-6-Catalyzed Reaction of "Naked" Cyanide with Alkyl Halides.

*The crown ring is represented as a circle for simplicity.

Although the corresponding "naked" fluoride and acetate systems followed a process similar to that shown in Figure 15 to give the normal reactivity order (bromides displaced faster than chlorides)[106,253-254], critical differences existed in comparison to the "naked" cyanide system. The most obvious was the relative reactivities of the anions toward the substrates, and thus the relative sizes of k^2. The second was that KF has a lattice energy 24.3 kcal/gfw higher than KCl, and thus the rate constant k^1_F in relation to k^{-3}_X would have a profound effect on the overall rate for the fluoride reagent. In support, KF has been found to have a solubility

limit of 3.5×10^{-3} M in a 0.16 M solution of 18-crown-6 in CH_3CN at 25°C[106].

Thus it was postulated that for "naked" fluoride, with the greater lattice energy (and hence lower complexing ability with 18-crown-6) of KF in relation to KCl or KBr, apparently shifted control of the overall rate of reaction to the rate constant k_F^2, i.e., k_{Cl}^{-3} were both so much greater in magnitude than k_F^1 that the overall rate was essentially independent of which salt was produced in the reaction. The "naked" fluoride selectively displaced the bromide more readily in the usual manner[485], and thus the relative magnitudes of k_F^2 on going from RBr to RCl determined the overall rate of reaction. With KCN, bromide was also displaced more readily than chloride until the catalytic crown ether was complexed with the KBr (as evidenced by the benzyl bromide and 1-bromo-3-chloropropane reactions). From that point, reaction slowed drastically due to the fact that $k_{Br}^{-3} \simeq k_{CN}^1$, and thus the overall rate of reaction was determined by the various equilibrium constants involving complexation of the crown with the 2 salts instead of k_{CN}^2. As $k_{CN}^1 >> k_{Cl}^{-3}$ due to the lattice energy differences, the reactions with alkyl chlorides were allowed to proceed readily to product, with the k_{CN}^2 constant essentially controlling the overall rate.

For potassium acetate in 0.14 M 18-crown-6 solution in CD_3CN, solubility was found to be 1×10^{-1} M[106], or roughly equivalent to that of KCN[488]. The answer for the

reversal of order of displacement with KOAc and KCN, therefore, originated in factors other than salt solubility, i.e., in the differences in selectivity of the 2 "naked" anions (rate constants k^2_{OAc} and k^2_{CN}). "Naked" acetate was apparently able to displace the bromide with far greater ease than the chloride[106,254], while the "naked" cyanide was not as selective. As a result, the overall rate for the "naked" acetate-alkyl bromide reaction was faster than with the chloride despite the salt complexation equilibria factors[106], while with less-selective "naked" cyanide, the latter controlled the overall rate.

The factors governing the relative rates of reaction of "naked" cyanide with alkyl halides were further elucidated by kinetic studies with homogeneous systems detailed elsewhere in this thesis. The conclusions detailed above were supported in the kinetic studies.

During the course of "naked" cyanide reactions with dihalides, glc peaks with retention times intermediate between the starting material and product were observed to grow to a maximum and then to decrease back to the base line before reaction was complete. Several reactions were thus halted, and the intermediate monocyanated products isolated and identified. The results are shown in Table 12. The mononitriles were produced as stable intermediates with or without 18-crown-6. The reaction with 1-bromo-3-chloropropane was especially interesting, as all possible products were obtained due to the crown's unique ability to complex and recomplex

Table 12. Products from the Incomplete Displacement of Primary Dihalides by "Naked" Cyanide in the Presence of 18-Crown-6.

Substrate	Solv.	Concentration[1] Crown (M)	Concentration[1] Substr. (M)	Temp.	Time $t_{1/2}$[2] (hr)	Time t_{stop}[3] (hr)	Products	Yield glc, nmr[4] (%)	Yield isolated[4] (%)
1,3-Dichloropropane	CH_3CN	0.15	1.8	Reflux	-	0.25	1-Chloro-3-cyanopropane	27	-
1,3-Dibromopropane	CH_3CN	0.15	1.8	Reflux	7	7	1,3-Dicyanopropane	16.5	-
							1-Bromo-3-cyanopropane	33	-
1-Bromo-3-chloropropane	CH_3CN	0.15	1.8	Reflux	-	8	1,3-Dichloropropane	-	7.5
							1-Bromo-3-chloropropane	-	11
							1,3-Dibromopropane	-	23
							1-Halo-3-cyanopropane[5]	-	4.5-6.5
							1,3-Dicyanopropane	-	-
1,4-Dichlorobutane	CH_3CN	0.0	1.8	Reflux	25	45	1,4-Dicyanobutane	-	33
							1-Chloro-4-cyanobutane	-	30

Table 12. Products from the Incomplete Displacement of Primary Dihalides by "Naked" Cyanide in the Presence of 18-Crown-6 (Continued).

Substrate	Solv.	Concentration[1] Crown (M)	Substr. (M)	Temp.	Time $t_{1/2}$[2] (hr)	t_{stop}[3]	Products	Yield glc, nmr[4] (%)	isolated[4] (%)
1,4-Dibromo-butane	CH_3CN	0.14	1.8	Reflux	6.5	7.7	1,4-Dicyano-butane	-	26
							1-Bromo-4-cyanobutane	-	46
1,4-Dibromo-butane	CH_3CN	0.0	1.8	Reflux	24	49	1,4-Dicyano-butane	87	-
							1-Bromo-4-cyanobutane	8	-

[1]The reactions were run in a total of 25 ml of solution, with a 2-fold excess of solid KCN per functional group converted.
[2]The time required for 50% of the starting material to react was defined as $t_{1/2}$.
[3]The time of reaction when the incompleted process was halted was designated as t_{stop}.
[4]The half-width band method[474] was used to determine the glc yield, with isolated yields for representative cases instead of internal standards used to validate the accuracy of the glc procedure. Nmr spectra (where applicable) exhibited only peaks for the stated products.
[5]The relative percentages of isolated 1-bromo- and 1-chloro-3-cyanopropane in the mixture could not be ascertained from glc and nmr data.

the various salts present in the system after reaction was initiated. Previous workers had reported isolation of only 1-chloro-3-cyanopropane[259] or a mixture of the mononitrile with 1,3-dicyanopropane[288] in similar reactions with cyanide.

The reaction of "naked" cyanide with cis-, trans-1,4-dichloro-2-butene also proved interesting, as a myriad of products were obtained. Figure 16 details possible mechanisms for the formation of 1-cyano-1,3-butadiene and cis-, trans-1,4-1- and 2-butenes (trans-1,4-dichloro-2-butene pictured). No logical explanation could be devised for the apparent production of small quantities of tetracyanobutanes in the reaction mixture. The identification of the tetracyanobutanes was open to question, however, as only sufficient solid for mass spectral analysis were isolated by glpc. The supporting analytical data for the cyanated butadiene and butenes are contained in Table 13, along with pertinent references. No evidence was found for production of 1,2,4-tricyanobutane, a possible product of hydrocyanation of the 1,4-dicyano-1-butenes. Also, as no 1-chloro-1,3-butadiene was detected, the "naked" cyanide was apparently too weak a base to abstract an allylic hydrogen activated only by a chloride. As shown in Figure 16, the allylic hydrogen of the nitrile-substituted methylene, however, was apparently acidic enough to be abstracted by the cyanide ion.

The substitution and elimination reactions of secondary halides with "naked" cyanide are detailed in Table 14. For

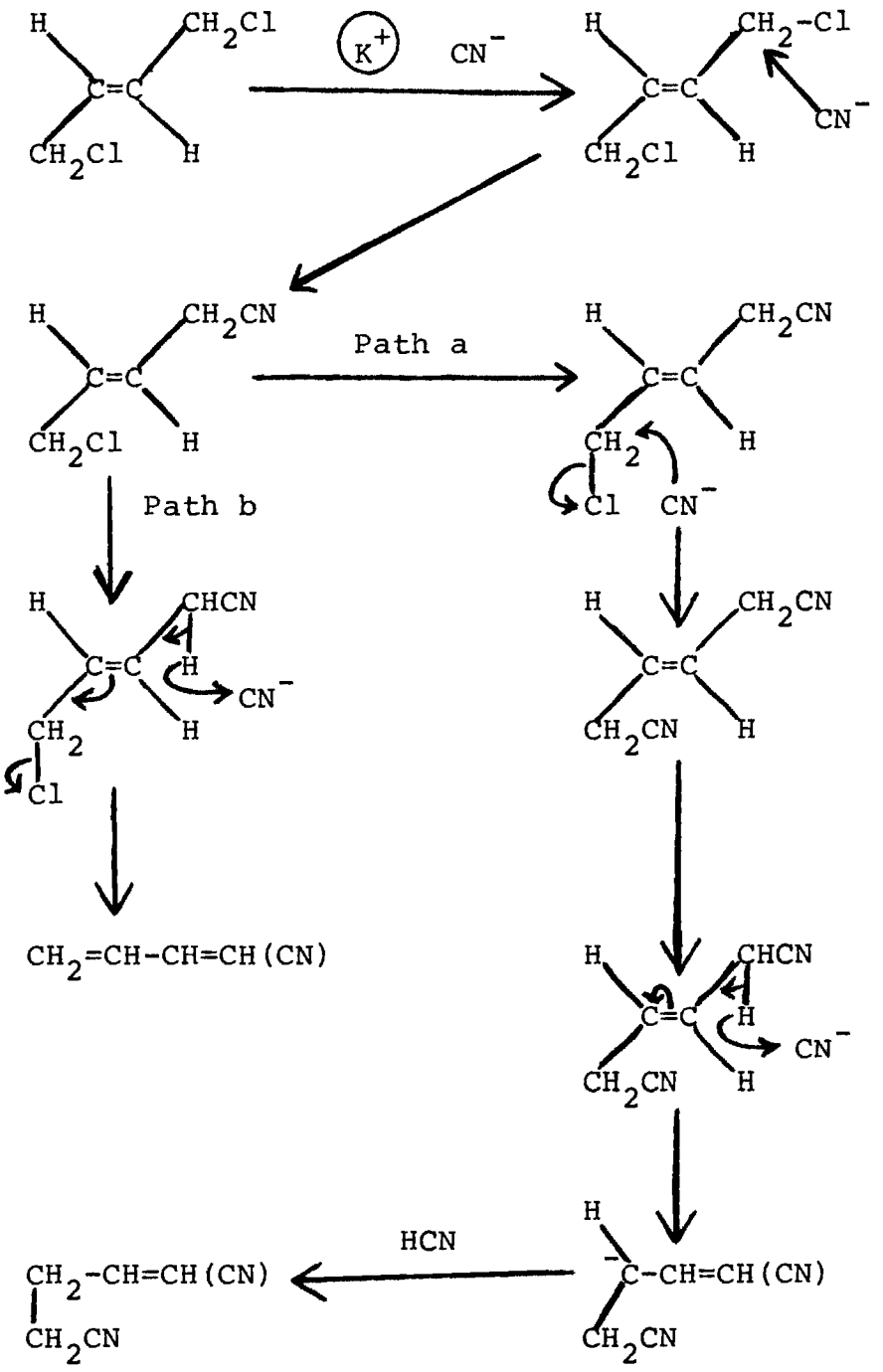


Figure 16. Possible Mechanisms for the Formation of Products Observed in the Reaction of "Naked" Cyanide with cis-, trans-1,4-Dichloro-2-Butene.

Table 13. Products Obtained from the Reaction of cis-, trans-1,4-Dichloro-2-Butene with "Naked" Cyanide in the Presence of 18-Crown-6.

	Supporting Analytical Evidence							Relevant References
	bp	mp	nmr	ms	glc	glpc	ir	
Cis-, trans-1-cyano-1,3-butadiene	x	-	x	x	x	x	-	339, 340
Cis-, trans-1,4-dicyano-1-butene	x	-	x	x	x	x	x	317, 341, 342
Cis-, trans-1,4-dicyano-2-butene	x	x	x	x	x	x	x	341, 357, 461
Tetracyanobutanes	-	-	-	x	x	x	-	None

Table 14. Substitution and Elimination Reactions of Secondary Halides with "Naked" Cyanide in the Presence of 18-Crown-6.

Substrate	Solv.	Concentration[1] Crown (M)	Concentration[1] Substr. (M)	Temp.	Time $t_{1/2}$[2] (hr)	Time $t_{com.}$[2] (hr)	Product	Yield glc, nmr[3] (%)	Yield isolated[3] (%)
2-Bromobutane	CH_3CN	0.14	2.0	Reflux	16	34	2-Cyanobutane	70	37
2-Bromobutane	C_6H_6	0.14	2.0	Reflux	62	66[4] 55[5]	2-Cyanobutane	43	-
2-Bromooctane	CH_3CN	0.12	2.0	Reflux	15	70	2-Cyanooctane Octenes[6]	62 17	56 -
2-Chlorooctane	CH_3CN	0.12	2.0	Reflux	59	220[4]	2-Cyanooctane Octenes[6]	78 3	- -
Cyclohexyl Bromide	CH_3CN	0.13	1.8	Reflux	-	54[4]	Cyclohexene[7]	46	-
Cyclohexyl Chloride	CH_3CN	0.15	1.8	Reflux	-	123[4]	Cyclohexene[7]	31	-

Table 14. Substitution and Elimination Reactions of Secondary Halides with "Naked" Cyanide in the Presence of 18-Crown-6 (Continued).

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[1]The reactions were run in a total of 25 ml of solution, with a 2-fold excess of solid KCN per functional group converted.
[2]The time required for 50% of the starting material to react was defined as $t_{\frac{1}{2}}$, and $t_{completion}$ was the time required for complete formation of the final product.
[3]The half-width band method[474] was used to determine the glc yield, with isolated yields for representative cases instead of internal standards used to validate the accuracy of the glc procedure. Nmr spectra (where applicable) exhibited only peaks for the stated product.
[4]These reactions were stopped before completion.
[5]Determination of $t_{\frac{1}{2}}$ made by nmr integration using the 18-crown-6 singlet as an internal standard.
[6]Consisted of a mixture of 1-octene and cis-, trans-2-octene by glc comparison with a known mixture[106]
[7]Identified by overlap of the olefin peak nmr absorption with a known sample[106].

the straight-chain secondary halides, the bromides reacted faster than the corresponding chlorides; however, less alkene and a higher overall yield of substitution product was obtained with the chloride. Difficulty was encountered in driving the reactions to completion. The difficulty may have originated in complexation of the crown with the eliminated acid, as Shchori and Jagur-Grodzinski have observed complexation of crown ethers with HBr in solution[222]. Such complexation would decrease the concentration of free 18-crown-6 (see the discussion above for primary nitriles), and hence slow the rate of reaction. HBr eliminates more readily than HCl, and hence a higher yield of substitution product with the secondary alkyl chloride was expected. Only cyclohexane was produced in the reaction with cyclohexyl halides, as has been observed with other systems[253-255]. The cyclohexene and octenes were identified by glc or nmr comparisons with known samples[106]. The octenes consisted of a mixture of 1-octene and cis-, trans-2-octenes by low-temperature comparison with the known mixture[106].

Addition and Addition-Elimination Reactions

The addition reactions performed with "naked" cyanide are located in Table 15. With catalytic "naked" cyanide present to initiate the process, the hydrocyanation of methacrylonitrile proceeded readily in the presence of acetone cyanohydrin (utilized as a proton donor and as a cyanide ion regenerator). The facile conversion of methacrylonitrile was somewhat surprising, as Michael acceptors usually contain substituted

Table 15. Addition Reactions Performed with "Naked" Cyanide in the Presence of 18-Crown-6.

Substrate	Solv.	Concentration[1] Crown (M)	Substr. (M)	Temp. (°C)	$t_{1/2}$[2] (hr)	$t_{com.}$	Product	Yield glc, nmr[3]	Yield isolated[3] (%)
Methacrylonitrile Acetone Cyanohydrin	CH_3CN	0.13	1.5 1.8	Reflux	0.3	0.6	1,2-Dicyanopropane	100	92
Methacrylonitrile Acetone Cyanohydrin	CH_3CN	0.13	1.5 1.7	Amb.	-	189[4]	1,2-Dicyanopropane	46	-
Methacrylonitrile Acetone Cyanohydrin	CH_3CN	0.0	1.5 1.7	Reflux	6	15	1,2-Dicyanopropane	100	77[5]
Cyclohexanone Acetone Cyanohydrin	C_6H_6	0.13	1.6 1.4	Reflux	-	2.7	Cyclohexanone Cyanohydrin	100[6]	39 (57)[7]
Cyclohexanone Acetone Cyanohydrin	C_6H_6	0.0	1.6 1.3	Reflux	-	3	Cyclohexanone Cyanohydrin	-	14 (70)[7]

Table 15. Addition Reactions Performed with "Naked" Cyanide in the Presence of 18-Crown-6 (Continued).

Substrate	Solv.	Concentration[1] Crown (M)	Concentration[1] Substr. (M)	Temp. (°C)	Time $t_{1/2}$[2] (hr)	Time $t_{com.}$	Products	Yield glc, nmr[3]	Yield isolated[3] (%)
Cyclohexanone	CH_3CN	0.13	1.5	Reflux	-	2	Cyclohexanone Cyanohydrin	100[6]	18
Acetone Cyanohydrin			1.7						

[1]The reactions were run in a total of 25 ml of solution, with a 2-fold excess of solid KCN per functional group converted.
[2]The time required for 50% of the starting material to react was defined as $t_{1/2}$, and $t_{completion}$ was the time required for complete formation of the final product.
[3]The half-width band method[474] was used to determine the glc yield for the hydrocyanations, with nmr showing only cyclohexanone cyanohydrin formed in the other reactions.
[4]This reaction was stopped before completion.
[5]The run was monitored frequently by glc, and thus a small quantity of 1,2-dicyanopropane was lost in the transfers.
[6]Nmr analyses of the crude reaction mixture showed complete conversion to cyclohexanone cyanohydrin.
[7]The figure in parentheses is the yield of cyclohexanone isolated on distillation of the reaction mixture, indicating the extent of reversal of the unstable cyanohydrin.

groups that stabilize the intermediate carbanion[302]. As shown in the chapters dealing with the synthesis of PAN models, methacrylonitrile was far less reactive than acrylonitrile in Michael additions due to the destabilizing effect of the electron-donating methyl group on the intermediate carbanion. Accordingly, the hydrocyanation proceeded extremely slowly at ambient temperatures (Table 15). In conjunction with earlier reports[318-321], acetone cyanohydrin alone was found to hydrocyanate methacrylonitrile. The rate, however, was much slower than in the presence of "naked" cyanide (Table 15).

An excellent yield of crude cyclohexanone cyanohydrin was obtained in the "naked" cyanide-acetone cyanohydrin system. However, reversal to starting material occurred to a large extent on attempted distillation. The instability of cyanohydrins has been the subject of numerous studies[380-389]. No attempt was made to stabilize the cyanohydrin to distillation *via* additives such as iodine[389]. Substantial improvement in the distilled yield was obtained by utilizing slightly less than 1 equivalent of cyanide ion (including both acetone cyanohydrin and KCN as sources). Apparently, trace CN^- in the crude reaction mixture was catalyzing the reversal in a chain reaction as shown in Figure 17.

Several reactions were attempted with "naked" cyanide that were not successful (Table 16). The unreactivity of *o*-dichlorobenzene toward the reagent was in contrast to the

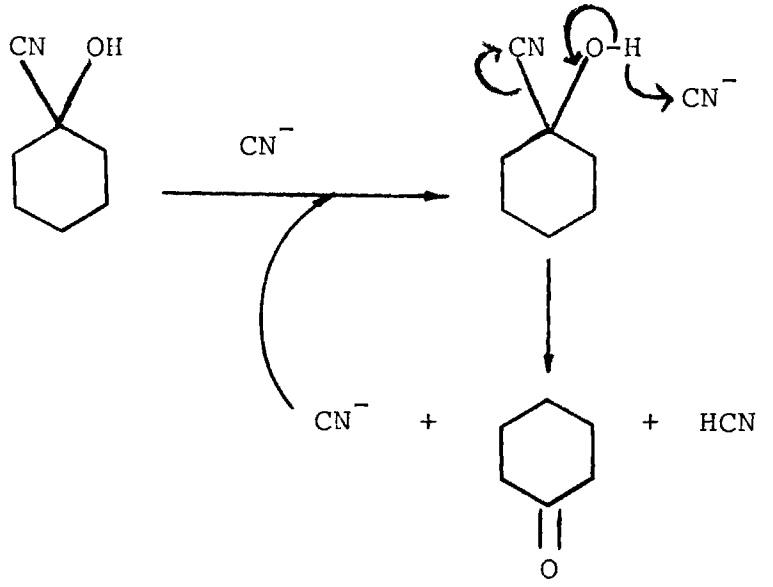

Figure 17. Reversal of Cyclohexanone Cyanohydrin to Cyclohexanone by Catalytic Cyanide Ion Attack.

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results reported for the analogous KOH-CH_3OH-crown system in which a 40-50% yield of o-chloroanisole was obtained[252]. The formation of tars with the various halobenzenes, with no substituted benzonitriles isolated or observed by glc, indicated that a complicated mixture of products such as those isolated from analogous reactions in KCN-DMSO was produced[301]. No benzoyl cyanide was synthesized[398], with high-melting crystalline solid isolated. As the mp was between those of benzoic acid and the dimer of benzoyl cyanide[398], a mixture of the 2 was probable. An nmr peak consistent with an acid proton confirmed the presence of $C_6H_5CO_2H$. Although no nmr evidence was observed for the formation of acetophenone or benzaldehyde cyanohydrins under homogeneous conditions, definite

Table 16. Reactions with "Naked" Cyanide in the Presence of 18-Crown-6 in which no Desired product was Produced.

Substrate	Solv.	Concentration Crown (M)	Concentration Substr. (M)	Temp. (°C)	Time (hr)	Desired Product	Remaining Start. Mat. (%)
o-Dichloro-benzene	CH_3CN	0.15	1.8	Reflux	109	2-Chloro-benzonitrile	100[1]
4-Chloro-nitrobenzene	CH_3CN	0.15	1.8	Reflux	101	4-Nitro-benzonitrile	54[2]
2,4-Dinitro-Chlorobenzene	CH_3CN	0.14	1.8	Reflux	1	2,4-Dinitro-benzonitrile	-
2,4-Dinitro-fluorobenzene	CH_3CN	0.14	1.8	20-25	21	2,4-Dinitro-benzonitrile	-
Benzoyl Chloride	CH_3CN	0.15	1.8	Amb.	2	Benzoyl Cyanide	-
Acetophenone	C_6H_6	0.51	0.49	Amb., -10-25	1	Acetophenone Cyanohydrin	100[1]
Benzaldehyde	C_6D_6	0.36	0.34	Amb.	0.5	Benzaldehyde Cyanohydrin	100[1]

[1]Remaining starting material as determined by glc or nmr.
[2]Reisolated starting material.

conclusions on possible reactivities of these substrates toward "naked" cyanide were not drawn as no effort was made to isolate the desired products in a synthetic procedure.

Several decarbalkoxylations were attempted with "naked" cyanide or chloride. The results are exhibited in Table 17. The reactions with diethyl phenylmalonate in benzonitrile proceeded at high temperatures, with "naked" cyanide giving a much higher yield of product than "naked" chloride in comparative runs. The yields obtained, however, were low in both cases compared to other systems[400,402]. A similar order of reactivity was reported for the decarbalkoxylation of 2-benzyl-2-carbmethoxycyclopentanone in HMPA with various sodium salts[401]. Ethyl-2,4-dicyanopentanoate, however, failed to decarbalkoxylate with "naked" chloride in refluxing CH_3CN or xylene-benzene, indicating the importance of solvent and reaction temperature on the tendency of reactive esters to decarbalkoxylate[400,402-403]. For a detailed discussion on the decarbalkoxylation of reactive esters, see the relevant sections in the chapters dealing with polyacrylonitrile models.

Kinetic Studies with "Naked" Cyanide

To validate the conclusions set forth for the reactions of "naked" cyanide with primary alkyl halides, kinetic studies were attempted for several representative substrates under homogeneous conditions. The critical questions to be answered were whether or not the actual displacement of bromide was faster than displacement of chloride by "naked" cyanide in

Table 17. Attempted Decarbalkoxylations with "Naked" Anions in the Presence of 18-Crown-6.

Substrate	Solv.	Salt	Concentration Crown (M)	Concentration Substr. (M)	Temp. (°C)	Time (hr)	Product	Yield glc, nmr[1]	Yield isolated[1] (%)
Diethyl Phenylmalonate	C_6H_5CN	KCN	0.11	1.8	180	9	Ethyl Phenylacetate	33 (16)[2]	30
Diethyl Phenylmalonate	C_6H_5CN	KCl	0.11	1.8	180	9	Ethyl Phenylacetate	6 (77)[2]	-
Ethyl-2,4-Dicyanopentanoate	CH_3CN	KCl	0.05	1.1	Reflux	16	1,3-Dicyanobutane	-	0[3]
Ethyl-2,4-Dicyanopentanoate	Xylene-Benzene	KCl	0.03	1.4	129	7	1,3-Dicyanobutane	-	0[3]

[1]The half-width band method[474] was used to determine the glc yield, with isolated yields for representative cases instead of internal standards used to validate the accuracy of the glc procedure. Nmr spectra (where applicable) exhibited only peaks for the stated product.
[2]The figures in parentheses are the percentages of starting material remaining.
[3]Based on no observed evolution of CO_2 by $BaOH-H_2O$ gas trap.

systems where solubility of salts produced or added was not a factor in the overall rate of reaction (Figure 15), and also whether or not the displacement was a true second-order (Sn2) process. The kinetic procedure is described fully in the Experimental chapter.

Benzyl chloride proved to be too reactive with "naked" cyanide under homogeneous conditions to obtain accurate kinetics. 1-Chlorohexane, however, reacted sufficiently slow at 49°C for the process to be monitored by the glc technique employed. White salt was observed to precipitate as the reaction progressed, denoting the low tendency of KCl to complex with 18-crown-6 in acetonitrile. The data obtained from the planimeter measurements of the reactant and product glc peaks at various times, along with the known concentrations at t_o, were substituted into the classical expression for second-order kinetics. A plot of t vs. ln $\left[b_o\ (a_o - x_n)\ /\ a_o\ (b_o - x_n)\right]$ for the equation:

$$k\ (a_o - b_o)\ t = \ln \left[\frac{b_o\ (a_o - x_n)}{a_o\ (b_o - x_n)} \right]$$

where:

k = second order rate constant (corresponding to k_{CN}^2 in Figure 15)

t = time of reaction

a_o = concentration of 1-chlorohexane at t_o (0.1756 M)

x_n= difference between the concentration of 1-chlorohexane at t_o and at t_n, $a_o - a_n$

b_o= initial concentration of "naked" cyanide ion, x_{end}.

is performed in Figure 18. From the visual plot a slope of 0.176 (slope equals k ($a_o - b_o$)) was obtained, yielding a rate constant of 4.6×10^{-4} liter/mole-sec. A linear regression program of a Wang 700 A/B Advanced Programming Calculator Computor plotted the "best" straight line for the data points, giving a slope of 0.183 and a corresponding rate constant of 4.8×10^{-4} liter/mole sec. The near-straight line obtained in the computer plot (>0.98 out of a possible 1.0 linearity rating assigned by the program) revealed conclusively that the reaction was second-order (Figure 18). The results were similar to those observed by Sams and Simmons for the displacement of n-BuOBs with various dicyclohexyl-18-crown-6-potassium salt complexes in acetone[252]. The displacements in the earlier study were also shown to be second-order, with rate constants varying from 9.72×10^{-3} 1/mole-sec for the KBr-crown complex to 2.32×10^{-3} 1/mole-second for the KI-crown complex[252]. The Sams-Simmons system was so different from that studied here that no conclusive correlations were possible. The Sn2 rate constants in the 2 investigations, however, were different only by approximately a factor of 10, with the "naked" cyanide displacement of primary chloride ion being slower than "naked" bromide or iodide displacement with the bromo substrate of primary brosylate ion[252].

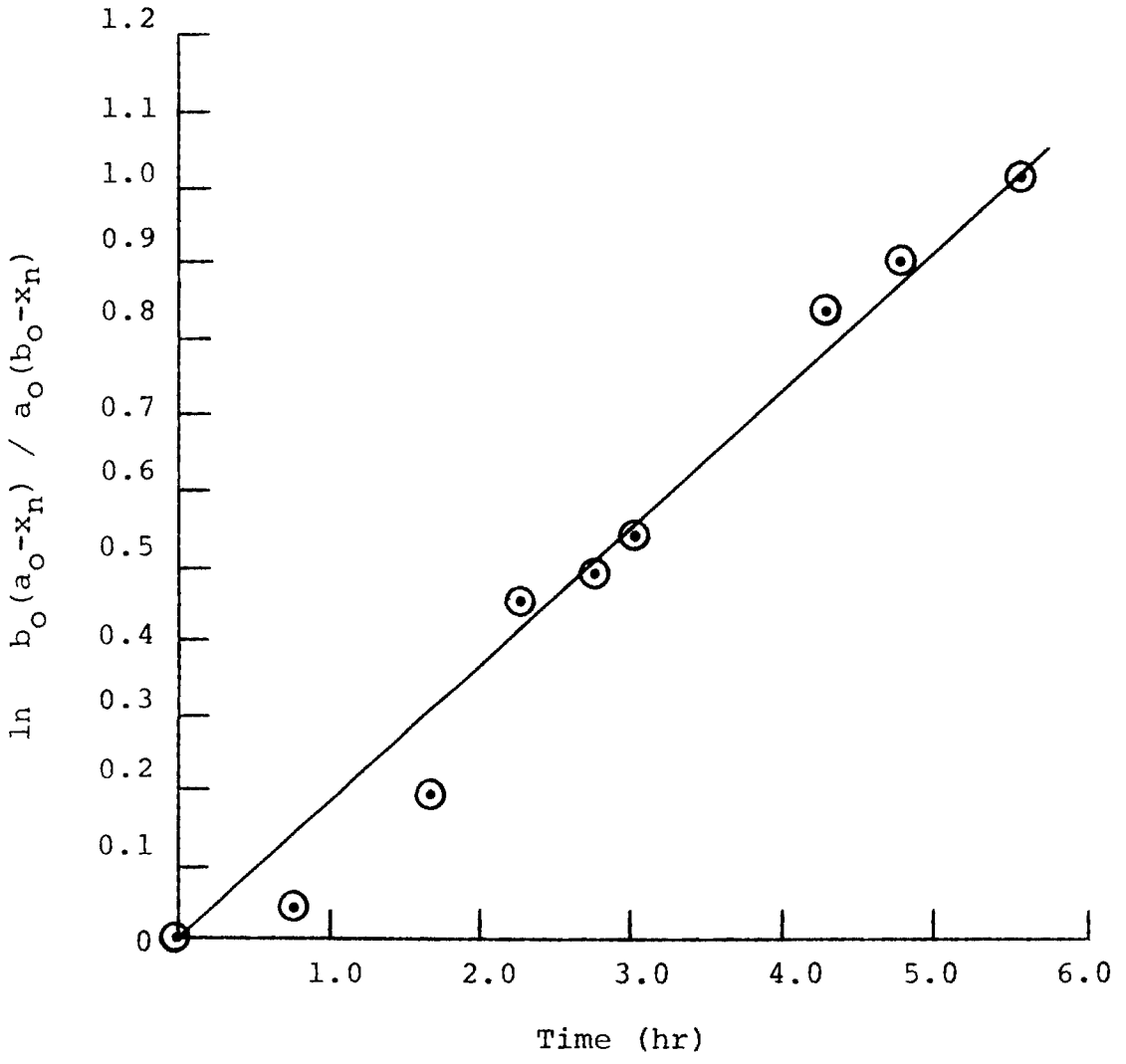

Figure 18. Second-Order Kinetic Plot of the Reaction of 1-Chlorohexane with "Naked" Cyanide under Homogeneous Conditions.

In a comparative run, 1-bromohexane was found to react much more rapidly with "naked" cyanide than had 1-chlorohexane. The displacement with the bromo substrate was 63% completed after 2-3 min at 25°C, and the substrate totally reacted at 0.2-0.4 hr at 49°C. (compare with Figure 18). Under homogeneous conditions, therefore, where the equilibrium constants governing the complexation-precipitation of the involved salts were not operating, the normal reactivity order was followed with "naked" cyanide (bromides faster than chlorides)[485]. In other words, k^2_{CN} was the only equilibrium shown in Figure 15 that was operating in the homogeneous system, and it alone controlled the overall rate.

Thus the kinetic results supported the conclusions based on observations made for the displacement of alkyl halides with "naked" cyanide utilizing catalytic 18-crown-6 and excess KCN (see the preceding section). The displacement was shown to be second-order with a rate constant of 4.8×10^{-4} liter/mole-sec for 1-chlorohexane, and with the displacement of bromide more readily accomplished than chloride displacement under homogeneous conditions, the postulate that the various salt equilibria in the catalytic crown synthetic system determined the overall rate of reaction was confirmed (Figure 15).

CHAPTER IX

CONCLUSIONS, CROWN ETHERS

Syntheses of Crown Ethers

A novel synthesis of 18-crown-6 was developed by G. W. Gokel and H. P. Harris with assistance by the author (Figure 11)[105-109] that resulted in a comparable yield of product to earlier methods[4,14,101-102]. Advantages over the earlier methods were the use of commercially available substrates, wet reaction conditions, and simplicity (both in reaction procedure and work-up)[108-109]. A unique feature of the developed synthesis was purification of the crude 18-crown-6 *via* the crown-acetonitrile complex. Unexplained violent behavior and poor yields resulted when recovered THF was substituted for commercial-grade solvent in the process. The 18-crown-6 synthesis has been published[108-109].

The first modified Williamson synthesis of 12-crown-4 without strictly anhydrous conditions and employing commercially-available substrates was also developed (Figure 12). The yield was comparable to that obtained by acid-catalyzed cyclic tetramerization of ethylene oxide, while the experimental procedure and work-up were simpler[119]. A tenacious complex or hydrate with water was formed on extraction, requiring stirring over molecular sieves to dry the crown. Ir spectra taken with NaCl plates indicated that complexation

occurred with the salt. Many systems proved unsuccessful in production of 12-crown-4, including direct cyclization of tetraethylene glycol *via* elimination of H_2O. The presented synthesis of 12-crown-4 has been published[131], and has received favorable reviews[478].

Adaptation of the developed 12-crown-4 reaction system to the synthesis of 14-crown-4 gave an impractical yield of desired cyclized product. The unsuccessful approach involved attempted formation of the monoadduct of 1,3-dichloropropane and ethylene glycol *in situ*, followed by coupling of 2 of the monoadducts to form the 14-crown-4 structure.

Complexes of 18-Crown-4 with Nitrile Compounds

Syntheses of Crown-Nitrile Complexes

Following discovery of the 18-crown-6-CH_3CN complex[106], a series of crystallin, high-melting 18-crown-6-nitrile compounds were synthesized and characterized (Table 6). A wide range of stoichiometries and melting points were exhibited, with the physical constants dependent on the nitrile precursor employed. The acetonitrile-crown complex was formed in 2 different physical forms, both of the same stoichiometry. The wide variation of molecular ratios, melting points, and physical forms of the various complexes indicated the unpredictable nature of the compounds. An uninterpretable relationship was obtained for the series of nitrile complexes with $NC(CH_2)_nCN$ nitriles, where n = 1, 2, 3, 4 (Figure 13). The sterically-hindered benzonitrile-crown complex was unstable,

while the complexes with acrylonitrile and δ-chlorovaleronitrile were also low-melting.

The analytical results indicated that the -C≡N group was not inserted directly into the "hole" of the cyclic polyether[215]. The low molecular ratios obtained dictated that clathrate-type inclusion complexes were not formed[218].

DTA/TGA, IR, and ^{13}C-NMR Analyses of Crown-Nitrile Complexes

Combined DTA/TGA, high-resolution ir, and ^{13}C-nmr analyses of the synthesized 18-crown-6-nitrile adducts signified that the crystalline solids satisfied the accepted definition as complexes[481]. No DTA transitions were observed below the endotherms associated with melting. Melting peaks obtained from the DTA endotherm peak corresponded well with those obtained by visual means (Tables 6 and 8). TGA studies exhibited a moderate loss of weight for the weak crown-CH_3CN complexes to the peak of the melting endotherm. The complexes derived from higher-boiling nitriles, however, were stable to the melting point. High-resolution ir analyses indicated a weakening of the nitrile triple bond on complexation. ^{13}C-nmr spectra exhibited small shifts of the crown methylene carbon and nitrile carbon absorptions on complexation in solution, denoting partial association[185,481]. DTA/TGA studies of pure 18-crown-6 indicated that the compound was thermally degrading above 120°C, signifying the undesirability of distilling the cyclic polyether from the complex and accounting for the observed wide boiling range for the impure

crown in the developed synthesis[105-109]. The syntheses and characterizations of the 18-crown-6-nitrile complexes have been submitted for publication[224].

Reactions Utilizing "Naked" Cyanide

Displacement and Elimination Reactions

The displacement of primary mono- and dihalides in CH_3CN with "naked" cyanide proceeded smoothly and mildly to high yields of product with no elimination (Table 11). Contrary to other systems (Appendix 2)[253-254,485], primary chlorides reacted much faster than corresponding bromides. The anomaly was attributed to control of the overall rate of reaction by equilibrium constants for the complexation-precipitation of the salts present in the system after initiation of reaction (Figure 15). This conclusion was confirmed by later kinetic studies under homogeneous conditions. Monocyanated products were isolated in runs involving difunctional halides with and without crown when the reactions were not allowed to proceed to completion (Table 12).

The reaction of cis-, trans-1,4-dichloro-2-butene with "naked" cyanide gave a myriad of products, including 1-cyano-1,3-butadiene, cis-, trans-1,4-dicyano-1 and 2-butenes, and small amounts of suspected tetracyanobutanes. Possible mechanisms for the observed products involved "naked" cyanide functioning as both a base and a nucleophile (Figure 16). Activation of the allylic hydrogens required presubstitution of chloride by cyanide ion, indicating the weakness of the cyanide base.

For the secondary halides, the bromides reacted faster than the corresponding chlorides (Table 14). A lower yield of olefin and a higher overall yield of substitution product was obtained with the latter, however, apparently due to a decreased tendency to eliminate HCl. Difficulty in driving the reactions to completion was attributed to complexation with the eliminated acids[222]. Only elimination product was obtained with cyclohexyl halides.

In comparison to earlier cyanation systems (Appendices 2 and 3), the "naked" cyanide procedure appeared to be superior to the EtOH-H_2O method in reaction time, simplicity of work-up, and yields. The presented procedure also compares favorably to the dipolar, aprotic solvent and phase-transfer catalyst (PTC) systems in both reaction time and yield for conversion of primary halides to nitriles, while affording lower reaction temperatures and improved simplicity of work-up. For secondary substrates, comparable yields to those presented in Table 14 were obtained in much shorter times for the DMSO and PTC systems, although reaction temperatures were higher. As pointed out by Brandstrom, the cheaper, more easily obtained alkyl chlorides are more-synthetically desirable than the corresponding bromides[268]. Most of the results with "naked" cyanide have been published[445].

Addition and Addition-Elimination Reactions

The hydrocyanation of methacrylonitrile proceeded at a rapid rate with catalytic "naked" cyanide and acetone

cyanohydrin at reflux (Table 15). Ambient temperatures or identical systems without 18-crown-6 resulted in drastically reduced rates of reaction. The procedure has been utilized to stereoselectively hydrocyanate cholestenone derivatives[488]. The yield of 1,2-dicyanopropane obtained from methacrylonitrile compared favorably with reported hydrocyanation reactions[302].

Formation of cyclohexanone cyanohydrin with "naked" cyanide and acetone cyanohydrin proceeded smoothly to a high yield of crude product (Table 15). Attempted distillation, however, caused substantial reversal to cyclohexanone via catalytic CN^- initiation of the process (Figure 17). Substantial improvement was obtained by using slightly less than 1 equivalent of cyanide ion. No marked improvement over existing methods was apparent[367, 378].

Several reactions attempted with "naked" cyanide were unsuccessful for various reasons (Table 16). Tars were obtained on reaction with activated halobenzenes, indicating a complicated mixture of products[301]. No nmr evidence was obtained for the formation of acetophenone or benzaldehyde cyanohydrins from the sterically-hindered carbonyls under homogeneous conditions. Attempted conversions of benzoyl chloride and o-dichlorobenzene to the corresponding nitriles also failed, the former giving undesired products and the latter not reacting[252,398]. The failure to form o-chlorobenzonitrile demonstrated that the "naked" cyanide was a weaker nucleophile than the "naked" methoxide ion of Sams and Simmons[252].

Decarbalkoxylation of ethyl phenylmalonate was achieved with "naked" cyanide and chloride in benzonitrile at high temperatures (Table 17). The yields were low, however, with the cyanide reagent catalyzing the reaction more effectively than "naked" chloride[401]. Ethyl-2,4-dicyanopentanoate failed to decarbalkoxylate with "naked" chloride in CH_3CN or xylene-benzene, apparently due to the low reflux temperatures and the comparatively low polarity of the solvents[400,402-403]. Work contained herein concerning decarbalkoxylation of reactive esters in wet DMSO has been published[402].

In summary, hydrocyanation and cyanohydrin-forming (unhindered ketones) reactions with naked cyanide were comparable to reported methods in yields and simplicity (Appendix 2)[302,367,378]. In addition, the hydrocyanation was more rapid than similar conversions performed in other systems[302].

Kinetic Studies with "Naked" Cyanide

Benzyl chloride and 1-bromohexane reacted too rapidly with "naked" cyanide under homogeneous conditions to obtain accurate kinetics. The corresponding reaction with 1-chlorohexane was much slower, and a second-order rate constant of 4.6 liter/mole-sec was obtained for the displacement reaction by a visual plot of the rate data (Figure 18). A plot of the "best" straight line for the data points by computer techniques gave a more-accurate second-order rate constant of 4.8×10^{-4} liter/mole-sec. The observance of second-order

kinetics, along with the faster displacement of bromides in the homogeneous system, confirmed the earlier conclusion that the various salt equilibria in the catalytic crown-"naked" cyanide synthetic system determined the overall rate of reaction.

CHAPTER X

RECOMMENDATIONS, CROWN ETHERS

Syntheses of Crown Ethers

The weak step in the developed 18-crown-6 synthesis was the distillation of the crown from the complex[105-109], with excessive fragmentation occurring (confirmed by ^{13}C-nmr). Separation of the crude crown from the complex might be accomplished by trans-complexation with acetonitrile in hot CCl_4 to deposit the metal salt, followed by work-up of the crown-CH_3CN complex as detailed. Other possible separatory techniques need to be explored. Utilization of the procedure to produce unsubstituted vinyl-18-crown-6, a potentially useful monomer, should be examined[48-53].

The weak link in the 12-crown-4 synthesis was in the necessity of placing the crude complex in water to rid the product of perchlorate compounds. As $LiClO_4$ is insoluble in chlorinated hydrocarbons[475], prolonged continuous extraction may improve the yield of 12-crown-4. Other, less-tenacious reaction solvents than DMSO should also be investigated, e.g., CH_3CN.

As the in situ 14-crown-4 procedure was unsuccessful, formation and isolation of the monoadduct of 1,3-dichloropropane and ethylene glycol would be a logical approach to the commercially-unavailable precursor of the crown. Once

synthesized, the monoadduct should cyclize readily to 14-crown-4 with the 12-crown-4 reaction system. Unsubstituted 14-crown-4 is postulated to be the optimum crown complexing agent for lithium[132].

Complexes of 18-Crown-6 with Nitrile Compounds

The spectrum of nitrile compounds as well as types of crown ethers should be expanded to determine the generality of crown-nitrile complex formation. Single-crystal X-ray studies are needed to elucidate the actual structures of the complexes[484]. The alteration of the chemical and physical properties of the complexed nitriles should also be investigated. Polymeric catenanes might be obtainable *via* radiation polymerization of the acrylonitrile monomers arranged in the crown complex[54], as well as stereoregular polymer.

Reactions Utilizing "Naked" Cyanide

Displacement and Elimination Reactions

The scope of the displacement reactions should be broadened to include more-complicated substrates than those examined herein. Solvent effects, perhaps with "naked" cyanide in more polar solvents such as DMSO, should be investigated[106]. Studies are needed to obtain a higher yield of substitution product for the secondary (straight-chain) alkyl halides and to find ways to drive the reactions to completion. Displacement of ions other than Cl^- or Br^- should also be attempted.

Addition and Addition-Elimination Reactions

The hydrocyanation system should be expanded to more-complicated substrates, as has been done with cholestenone derivatives[448], to determine the generality of the reaction. A concentrated effort should also be made to modify the distillation procedure of crude cyanohydrins produced with "naked" cyanide to reduce reversal. Attempts to isolate and identify products from the complicated mixture obtained in the "naked" cyanide-acetivated halobenzene systems should also be attempted. The effect of catalytic 15-crown-5 on the decarbalkoxylation rate of unreactive esters[403] with wet DMSO-NaCl or NaCN needs to be examined.

Kinetic Studies with "Naked" Cyanide

The type of substrates kinetically examined with "naked" cyanide under homogeneous conditions should be expanded. Rate studies with secondary halides should prove especially interesting, as would studies with leaving groups other than chloride or bromide.

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Appendix 1. Systems Investigated from which no 12-Crown-4 was Isolated.

Dihalide	Glycol	Solvent	Salts	Temp. (°C)	Time (hr)
2-Chloroethyl-ether	2-Hydroxyethyl-ether	THF, H_2O	KOH, LiCl	Reflux	15
2-Chloroethyl-ether	2-Hydroxyethyl-ether	THF, H_2O	$LiOH \cdot H_2O$	Reflux	15
2-Chloroethyl-ether	2-Hydroxyethyl-ether	THF, H_2O	NaOH	Reflux	16
1,2-Dibromo-ethane	Triethylene glycol	THF, H_2O	NaOH	Reflux	15.5
1,2-Dibromo-ethane	Triethylene glycol	dry THF (N_2)	$K^+t\text{-}BuO^-$, $LiClO_4$	35-40* 60	15 22
1,2-Dibromo-ethane	Triethylene glycol	dry THF (N_2)	$Li^+t\text{-}BuO^-$	40* 60	29 29
1,2-Dibromo-ethane	Triethylene glycol	Dioxane, H_2O	NaOH	Reflux	24
1,2-Dibromo-ethane	Triethylene glycol	DMSO, H_2O	$LiOH \cdot H_2O$	80	20
3,6-Dioxa-1,8-dichlorooctane	Ethylene glycol	DMSO	$LiOH \cdot H_2O$	110	20

Appendix 1. Systems Investigated from which no 12-Crown-4 was Isolated (Continued).

Dihalide	Glycol	Solvent	Salts	Temp. (°C)	Time (hr)
3,6-Dioxa-1,8-dichlorooctane	Ethylene glycol	DMSO	NaOH	110	22
1,2-Dibromoethane	Triethylene glycol	DMSO	NaOH $LiClO_4$	110	22
1,2-Dibromoethane	Triethylene glycol	DMSO	NaOH	110	22
- -	Tetraethylene glycol	DMSO	$LiClO_4$	160	18
-	Tetraethylene glycol	DMSO	-	160	18

*Denotes 2 runs conducted under different conditions with the same reaction system.

Appendix 2. Representative Literature Preparations of Primary Nitrile Compounds.

Reagent	Ref.	Salts	Solv.	Conditions Temp. (°C)	Conditions Time (hr)	Products	Yield (%)
Benzyl Chloride	288	$C_6H_5\overset{+}{N}(CH_3)_3Cl^-$ (10%), NaCN	CH_2Cl_2, H_2O	95	0.2	Benzyl Cyanide	92
"	258	NaCN	EtOH, H_2O	100	4	"	80-90
"	276	NaCN	DMSO	35-40	2.5	"	92
"	292	Resin, CN Form	EtOH	65-75	3	"	62
Benzyl Bromide	291	Resin, CN Form	C_6H_6	65-75	2	"	72
1-Chlorooctane	289	$C_{16}H_{33}\overset{+}{P}(Bu)_3Br^-$ (1%), NaCN	Reag., H_2O	105	3	1-Cyanooctane	95
1-Bromooctane	289	"	"	"	1.5	"	"
1-Bromobutane	266	NaCN	Ethylene Glycol	101	1	1-Cyanobutane	90
"	269	NaCN, Cat. KI	Cellusolve, H_2O	Reflux	4.6	"	69
"	276	NaCN	DMSO	60-90	0.6	"	92

Appendix 2. Representative Literature Preparations of Primary Nitrile Compounds (Continued).

Reagent	Ref.	Salts	Solv.	Conditions Temp. (°C)	Time (hr)	Products	Yield (%)
"	288	$C_6H_5\overset{+}{N}(CH_3)_3Cl^-$ (10%), NaCN	CH_2Cl_2, H_2O	90	6	"	71.4
1-Chlorobutane	269	NaCN, cat. KI	Cellusolve, H_2O	Reflux	4	1-Cyanobutane	12
1,3-Dibromo-propane	260	NaCN	EtOH, H_2O	100	30-60	1,3-Dicyano-propane	77-86
1,3-Dichloro-propane	275	NaCN	DMSO	160	0.5	"	67
1-Bromo-3-chloropropane	259	KCN	EtOH, H_2O	100	1.5	1-Chloro-3-cyanopropane	40-47
"	288	$C_6H_5\overset{+}{N}(CH_3)_3Cl^-$ (10%), NaCN	CH_2Cl, H_2O	90	1.5	"	48
						1,3-Dicyano-propane	23
"	"	"	"	"	6	1-Chloro-3-cyanopropane	52
						1,3-Dicyano-propane	25

Appendix 2. Representative Literature Preparations of Primary Nitrile Compounds (Continued).

Reagent	Ref.	Salts	Solv.	Conditions Temp. (°C)	Conditions Time (hr)	Products	Yield (%)
1,4-Dichloro-butane	275	NaCN	DMSO	160	0.5	1,4-Dicyano-butane	88
"	267	NaCN	t-BuOH, Ethylene Glycol	100	5	"	92

Appendix 3. Representative Literature Preparations of Nitriles Other Than Primary Substituted Compounds.

Reagent	Ref.	Salts	Solv.	Conditions Temp. (°C)	Conditions Time (hr)	Products	Yield (%)
Benzoyl Chloride	398	$\overset{+}{N}(t\text{-Bu})_4\overset{-}{Br}$ (cat.), NaCN	CH_2Cl_2 H_2O	0	1	Benzoyl Cyanide Dimer	60 35
2-Bromobutane	276	NaCN	DMSO	70	6	2-Cyanobutane	41
"	266	"	Ethylene Glycol	92	4	"	28
"	277	"	CH_3OH, H_2O	-	65	"	45
"	"	"	Diglyme	-	34	"	10
"	275	"	DMSO	150	3	"	69
2-Chlorooctane	289	$C_{16}H_{33}\overset{+}{P}(Bu)_3\overset{-}{Br}$ (1%), NaCN	Reag., H_2O	105	-	2-Cyanooctane	85-90
"	275	NaCN	DMSO	145	1	"	70
p-Chloronitro benzene	301	KCN	DMSO	100	2	5 Products	40 (comb.)

Appendix 3. Representative Literature Preparations of Nitriles Other Than Primary Substituted Compounds (Continued).

Reagent	Ref.	Salts	Solv.	Conditions Temp. (°C)	Conditions Time (hr)	Products	Yield (%)
Cyclohexanone Acetone Cyanohydrin	378	Cat. K_2CO_3-MeOH	Neat	20	12	Cyclohexanone Cyanohydrin	86
Cyclohexanone	367	KCN	H_2O-Ac_2O	25	14	"	76

APPENDIX 4

PUBLISHED PAPERS

Tetrahedron Letters No. 13, pp 1095 - 1096, 1974. Pergamon Press. Printed in Great Britain.

CONCERNING THE DECARBALKOXYIATIONS OF GEMINAL DIESTERS, β-KETO ESTERS AND α-CYANO ESTERS EFFECTED BY SODIUM CHLORIDE IN WET DIMETHYL SULFOXIDE

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Krapcho and Lovey[1] have recently reported a facile decarbalkoxylation of geminal diesters, β-keto esters and α-cyano esters in excellent yields by sodium chloride in wet dimethyl sulfoxide at temperatures ranging from 120-183°C. A mechanism involving nucleophilic attack of chloride ion on the carbonyl carbon followed by elimination to form ethyl chloroformate and a stabilized carbanion was proposed. We wish to report that the presence of sodium chloride is unnecessary to effect chemical reaction for several reactive substrates and therefore the suggested mechanism is probably not general.

The decarbalkoxylation reactions were carried out on ethyl cyanoacetate, ethyl phenylmalonate and 2-carbethoxycyclopentanone[2] by procedures similar to those described by Krapcho and Lovey only in the absence of sodium chloride.[3] The isolated yields of acetonitrile, ethyl phenylacetate and cyclopentanone were 78-80%,[4] 93-96% and 75-80%, respectively, in good agreement with those reported by the above workers. These observations are consistent with a mechanism involving hydrolysis of the ester function followed by decarboxylation of the resulting cyano acid, ester acid or keto acid.

While sodium chloride appears to be an unnecessary reagent in decarbalkoxylation reactions of reactive substrates, it should be emphasized that the modified procedure of Krapcho and Lovey (use of wet dimethyl sulfoxide only) represents an excellent method of carrying out these transformations.[5]

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of the Interior, Office of Water Resources Research, as authorized under the Water Resources Research Act of 1964, and by the National Science Foundation (Grant No. GP 1437). A Tennessee Eastman Fellowship to FLC, administered by the School of Textile Engineering (Georgia Institute of Technology), is gratefully acknowledged.

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2. Analysis of nmr indicated that the sample of 2-carbethoxycyclopentanone contains 63% ethyl ester and 37% methyl ester. The reported yields were based upon this percent mixture.

3. The initial temperatures at which carbon dioxide evolution commenced and the final temperatures are as follows: (a) ethyl cyanoacetate: 150° and 142°C (135° and 165°C). (b) ethyl phenylmalonate: 146° and 155°C (135° and 170°C). (c) 2-carbethocyclopentanone: 120° and 142°C (120° and 150°C). The temperatures in the parantheses are the corresponding values reported by Krapcho and Lovey. The slight descrepancies could lie in the colligative property effect of the dissolved sodium chloride which would tend to raise the boiling point of the pot liquid. A decarbethoxylation reaction was carried out with ethyl phenylmalonate in which the lower boiling components (water and ethanol) in the pot were distilled off during the course of reaction. The initial and final temperatures in this case were 146° and 175°C, respectively, which are closer to the corresponding values reported by Krapcho and Lovey.[1] 94% isolated yield of ethyl phenylacetate was obtained.

4. Krapcho and Lovey[1] reported yields of 85-95%; however, they commented that the acetonitrile was contaminated with ethanol and a little dimethyl sulfoxide. The 78-80% reported in this communication represents the actual yield of acetonitrile as determined from nmr analysis.

5. Krapcho and co-workers[6,7] have also employed sodium cyanide in dry dimethylsulfoxide to effect decarbethoxylations of geminal diesters. This method has been successfully employed by several workers.[8,9] We have carried out the decarbethoxylation of ethyl phenylmalonate in dry dimethylsulfoxide in the absence of sodium cyanide. The pot temperature at which carbon dioxide evolution commenced was 178°C. The temperature then rose to 190°C and then slowly decreased to 163°C. The evolution of carbon dioxide ceased after approximately 10 hours and a 75-80% isolated yield of ethyl phenylacetate was obtained. Based upon these results, the need for sodium cyanide is questionable when dealing with reactive substrates. Comparison of the methods using dry DMSO and wet DMSO to effect decarbalkoxylation reactions indicated that the latter is the preferred method since the reaction since the reaction temperatures are lower and the reaction times somewhat shorter. It should be emphesized that the mechanism for decarbalkoxylation is not necessarily the same in dry and wet DMSO.

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Preparation and Purification of 18-Crown-6[1]

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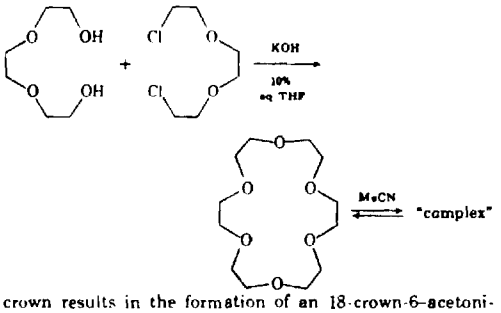
Of the many crown ethers which have been prepared[2] since the pioneering work of Pedersen[3] first appeared, 18-crown-6 is probably the simplest and most synthetically useful. Its synthesis in low yield was reported by Pedersen in his first paper.[3] Greene[4] and Dale and Kristiansen[5] have reported syntheses of 18-crown-6 from triethylene glycol and the corresponding ditosylate. A variety of bases was examined by Greene[4] but in both cases potassium *tert*-butoxide was favored. We report here a simple synthesis of 18-crown-6 from triethylene glycol and the commercially available (Eastman) 3,6-dioxa-1,8-dichlorooctane (triethylene glycol dichloride) using potassium hydroxide as base in 10% aqueous tetrahydrofuran and purification of the crown *via* its acetonitrile complex.

The Williamson ether synthesis yields crude crown in about 40% yield after a rapid distillation under high vacuum. The distilled material contains an impurity believed to he a vinyl ether and some open-chain, hydroxyl-containing material. Addition of acetonitrile to the crude



crown results in the formation of an 18-crown-6–acetonitrile adduct (complex)[6] of variable stoichiometry depending on conditions. Evaporation of the acetonitrile leaves crown of high purity. Evidence on the nature of this and other complexes of 18-crown-6 will be published elsewhere.

Experimental Section

A 3-l., three-neck flask equipped with mechanical stirrer, reflux condenser, and addition funnel was charged with triethylene glycol (112.5 g, 0.75 mol) and tetrahydrofuran (600 ml). Stirring was commenced and a 60% KOH solution (109 g of 85% KOH in 70 ml of water) was poured in. The solution warmed but did not boil. After *ca.* 15 min of stirring (the solution darkened) a solution of 3,6-dioxa-1,8-dichlorooctane (140.3 g, 0.75 mol) in THF (100 ml) was added in a stream. After the addition was complete, the solution was heated at reflux and stirred vigorously for 18 hr. The solution was allowed to cool and the bulk of the THF was evaporated under reduced pressure. The resulting thick brown slurry was diluted with 500 ml of dichloromethane and filtered. The salts removed by filtration were washed with more dichloromethane to remove adsorbed crown, and the combined organic solution was dried over $MgSO_4$, evaporated to minimum volume (aspirator vacuum), and then distilled under high vacuum. The distillation should be carried out at the lowest possible pressure; a typical fraction contained 80 g and was collected at 100–160° (0.2 mm).

To 50 g of crude 18-crown-6, bp 125–160° (0.2 mm), in a 250-ml erlenmeyer flask was added 125 ml of acetonitrile. The resulting slurry was heated on a hot plate to effect solution. A magnetic stirring bar was added and the neck was equipped with a $CaSO_4$ drying tube. The solution was stirred vigorously as it was allowed to cool to ambient temperature, and fine white crystals of crown–acetonitrile complex were deposited. The flask was finally cooled in an ice–acetone bath to precipitate as much complex as possible, and the solid was then collected by rapid filtration. The hygroscopic crystals were transferred to a 500-ml round-bottom flask equipped with a magnetic stirring bar and vacuum take-off. The acetonitrile was removed from the complex under high vacuum (0.1–0.5 mm) with gentle heating (≤40°) over 2–3 hr. The pure, colorless crown (20–30 g, 40–60%) crystallized on standing and showed no ions above m/e 265 in the mass spectrum and no significant hydroxyl vibration in the 3500-cm^{-1} region of the infrared. The pure crown had mp 36.5–38.0° (lit.[4] mp 39–40°); nmr (60 MHz, CCl_4) 3.56 ppm (singlet); ir (neat) 2875 (alkane CH), 1450 and 1350 (alkane CH), and 1120 cm^{-1} (ether link); mass spectrum M and M + 1 at m/e 264 and 265, other fragments at m/e 89, 87, 59, 45, 44, 43, and 31.

Registry No.—18-Crown-6, 17455-13-9; triethylene glycol, 112-27-6; 3,6-dioxa-1,8-dichlorooctane, 112-26-5.

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(6) A number of solid complexes of crown ethers are reported, including complexes of many metal ions,[2a] hydronium ion,[7] bromine,[8] thiourea,[9] and others. With the exception of the metal ions where a crystal structure has been determined, the nature of the interactions between host and guest is not clearly understood. There is an obvious possibility that different substrates interact differently with the host, affording on different occasions a complex, a solvate, and so on. Intuitively, it appears that two possible factors favor formation of a host-guest solid adduct. The large size of the 18-membered ring and its lack of rigidity might favor the interstitial trapping of other molecules to gain a more favorable crystal lattice. The second factor which probably influences the formation of such complexes is the multiplicity of electronegative heteroatoms distributed in the ring system which have the potential for interacting with and further ordering, the guest molecule in the lattice. We therefore use the term "complex" advisedly and are aware that probably only structural data derived from direct observations (*e.g.*, X-ray) will resolve the nature of the complex in individual cases.
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Chemistry of "Naked" Anions. III. Reactions of the 18-Crown-6 Complex of Potassium Cyanide with Organic Substrates in Aprotic Organic Solvents[1,2]

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Following Pedersen's discovery that macrocyclic polyethers ("crown" ethers) possess the ability to form crystalline complexes with a variety of inorganic salts and also the ability to solubilize these salts in aprotic organic solvents,[1] attention has been gradually focused toward utilizing the anion of the complex for synthetic purposes.[4] It has recently been reported that poor nucleophiles such as fluoride and acetate ions, solubilized as the potassium salt in CH_3CN or C_6H_6 containing 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane, 1),[1] become sufficiently nucleophilic to react smoothly and quantitatively with a variety of organic substrates.[1,2] These reactive species have been termed "naked" anions.[1] We now wish to report the preparation of the "naked" cyanide reagent and its utilization in a variety of synthetically useful reactions. Substitution, elimination, and addition processes have been explored.

The results are summarized in Table I. The reactions were carried out by simply pouring a substrate–crown solution directly over excess, dry KCN, and stirring the two-phase system vigorously at ambient or reflux temperature until reaction was complete. Little or no reaction was found to take place in the absence of 1 under the same conditions covering the same periods of time (runs 20 and 21, Table I). In all cases, 1 was present in catalytic quantities, indicating that it behaves as a phase-transfer catalyst.[5] In general, the reactions are more rapid in CH_3CN than in C_6H_6.

The reaction of "naked" cyanide with benzyl chloride proceeded quickly and quantitatively to product under mild conditions (run 20, Table I). With primary-substituted alkyl halides, the conversions to nitrile compounds were quantitative, with no elimination products detected (runs 1–12, Table I).[6] Displacement at secondary carbon produced primarily substitution products with only a small percentage of elimination products. These results compare favorably to those obtained with "naked" acetate,[2] but are in direct contrast to those of "naked" fluoride,[1] where large quantities of alkenes were obtained. It appears therefore, that "naked" fluoride may be a stronger base than either "naked" cyanide or "naked" acetate. Cyclohexyl halides gives exclusively elimination product with "naked" cyanide (runs 17 and 18, Table I). No reaction was observed with *o*-dichlorobenzene (run 22, Table I).

Table I[a]
Reactions of "Naked" Cyanide with Organic Substrates in the Presence of 18-Crown-6

Substrate	Registry no.	Run	Solvent	Products (yield, %)	Registry no.	Concn, M[b] Crown	Concn, M[b] Substrate	Temp, °C	$t_{1/2}$,[c] hr	t_{read}, hr
1,3-Dibromopropane	109-64-8	1	CH_3CN	Glutaronitrile (97.3)[d]	544-13-8	0.151	1.80	83	7	25
		2	CH_3CN	Glutaronitrile (94.9)[d]		0.147	1.80	Ambient	10.5	48
		3	C_6H_6	Glutaronitrile (100)[e]		0.147	1.80	90	12	40
		4	C_6H_6	Glutaronitrile (100)[e]		0.147	1.80	Ambient	10	49
1-Bromo-3-chloropropane	109-70-6	5	CH_3CN	Glutaronitrile (100)[e]		0.152	1.80	83	1.1	30
1,3-Dichloropropane	142-28-9	6	CH_3CN	Glutaronitrile (96.8)[d]		0.154	1.80	83	0.23	1.5
1,4-Dibromobutane	110-52-1	7	CH_3CN	Adiponitrile (100)[e]	111-69-3	0.141	1.80	83	6.5	14.5
		8	CH_3CN	Adiponitrile (100)[e]		0.141	1.80	Ambient	11	57
1,4-Dichlorobutane	110-56-5	9	CH_3CN	Adiponitrile (94.7)[d]		0.144	1.80	83	0.2	0.7
		10	CH_3CN	Adiponitrile (86)[d]		0.144	1.80	Ambient	8	75
1-Bromohexane	111-25-1	11	CH_3CN	1-Cyanohexane (100)[e]	629-08-3	0.138	1.80	83	10	40
1-Chlorohexane	544-10-5	12	CH_3CN	1-Cyanohexane (90.6)[d]		0.139	1.80	83	0.5	2.2
2-Bromobutane	78-76-2	13	CH_3CN	2-Cyanobutane (69.7)[e]	18936-17-9	0.141	2.00	83	18	32
		14	C_6H_6	2-Cyanobutane (43.4)[e]		0.140	2.01	90	58	66[f]
2-Bromooctane	557-35-7	15	CH_3CN	2-Cyanooctane (56)[d] (62)[e] -octene (17)[d,g]	2570-96-9	0.119	2.00	83	14	78
2-Chlorooctane	628-61-5	16	CH_3CN	2-Cyanooctane (77.5)[e,h] -octene (3.1)[e,g,h]		0.122	2.00	83	59	244[h]
Cyclohexyl bromide	108-85-0	17	CH_3CN	Cyclohexene (46)[e,i]	110-83-8	0.132	1.80	83		53[f]
Cyclohexyl chloride	542-18-7	18	CH_3CN	Cyclohexene (32)[e,i]		0.146	1.80	83		122.5[f]
Benzyl bromide	100-39-0	19	CH_3CN	Benzyl cyanide (100)[e]	140-29-4	0.146	1.80	Ambient	13	25
Benzyl chloride	100-44-7	20	CH_3CN	Benzyl cyanide (94.2)[d]		0.147	1.80	Ambient	0.08	0.4
		21	CH_3CN	Benzyl cyanide (20)[e,j]		0.0	1.80	Ambient		75[f]
o-Dichlorobenzene	95-50-1	22	CH_3CN	No reaction[e]		0.145	1.80	83		109
Methacrylonitrile (Acetone cyanohydrin)[k]	126-98-7	23	CH_3CN	1,2-Dicyanopropane (91.9)[d,l]	623-35-8	0.132	1.51 (1.78)	83	0.3	0.6
		24	CH_3CN	1,2-Dicyanopropane (46)[e,l]		0.132	1.52 (1.72)	Ambient		189[f]
		25	CH_3CN	1,2-Dicyanopropane (77)[d,m]		0.0	1.51 (1.74)	83	6.1	15.5

[a] For the isolated products, nmr, ir, and mass spectral data confirmed the pure compound's identity. Also, where possible, these spectra and glc data of the products were compared to those of the commercial compounds (runs 1–12). [b] The reactions were run in a total of 25 ml of solution, with a twofold excess of solid KCN per functional group for the substitution reactions, and a catalytic amount (approximately equivalent to 18-crown-6) of salt for the hydrocyanation. [c] $t_{1/2}$ is defined as the time required for 50% of the starting material to react. [d] Isolated yields. For these examples, glc and nmr analysis showed a quantitative conversion to the products. [e] Calculated from glc and nmr data. [f] In these runs, the reactions were stopped before completion. [g] From glc analysis, 1-octene and both *cis*- and *trans*-2-octene were formed. [h] There was difficulty in driving the reaction to completion. At 244 hr, the composition consisted of 7.4% starting material, 89.1% substitution product, and 3.5% olefin by glc analysis. The yields given in Table I are thus based on reacted starting material. [i] The absence of reaction of "naked" cyanide with o-dichlorobenzene was in contrast to the results recently reported for the analogous KOH-CH_3OH-crown system in which a 40–50% yield of o-chloroanisole was obtained.[4a] [j] 1.18 molar equiv of acetone cyanohydrin was used. It functioned as a proton donor and a cyanide ion regenerator after initiation of the reaction by the "naked" cyanide. [k] Run 25 was monitored frequently during the course of the reaction by glc, and thus a small quantity of product was lost in the transfers. The reaction was quantitative by glc and nmr analyses. [l] Reference 18.

Interestingly, primary chlorides react much faster than the corresponding bromides under the reaction conditions. For example, benzyl chloride reacts about 100 times faster than benzyl bromide (runs 19 and 20, Table I). This observation is contrary to the normally accepted leaving group order.[7] It is also opposite to what has been observed with "naked" acetate and "naked" fluoride.[1,2] With the secondary halides, it appears that bromides react more rapidly than chlorides; however, less alkene[8] and a higher overall yield of substitution product are obtained with the chloride. The causes of these observations are currently being investigated. It is emphasized here, however, that for synthetic purposes chlorides are preferred over bromides under the reaction conditions reported.

Substitutions of halides by cyanide ion have been reported to occur (1) in ethanol–water mixtures under strenuous conditions;[10] (2) in dipolar, aprotic solvents such as DMSO;[11] and (3) by use of tetraalkylammonium or -phoaphonium salts to transfer the cyanide ion across a water–organic interface (phase-transfer catalysis).[5,12] Comparatively, the "naked" cyanide system appears to be superior to the ethanol–water method in reaction time, temperature, simplicity of work-up, and yields.[10,13] It also compares favorably to the dipolar, aprotic solvent and phase-transfer catalyst systems in both reaction time and yield for conversion of primary halides to nitriles.[11,12] Advantages of the "naked" cyanide procedure over these latter methods are lower reaction temperature and simplicity of work-up. For secondary substrates, comparable yields to those presented in Table I were obtained in much shorter times in the dipolar, aprotic solvent,[11b] while the phase-transfer catalyst system gave a higher yield of substitution product (no reaction time was reported).[12a] The reaction temperatures, however, were higher in both the DMSO and phase-transfer catalyst systems.[11,12]

The quantitative hydrocyanation reaction (run 23) is included to demonstrate the versatility of the "naked" cyanide reagent. In the absence of crown, reaction was found to proceed at a comparatively slow rate (run 25). The yield obtained in run 23 compares favorably with reported hydrocyanation reactions.[14]

In summary, it has been shown that 1 effectively solubilizes KCN in aprotic solvents, that the resulting "naked" cyanide is both a weak base and a potent nucleophile, and that the reagent produces nitrile compounds smoothly, mildly, and in high yields from a variety of organic substrates.

Experimental Section

The following instruments were used in the analyses: a Varian Model 90-P gas chromatograph for glc analyses, a Varian Model M-66 mass spectrometer for mass spectra, a Varian Model A-60 or T60-A nuclear magnetic resonance spectrometer for nmr spectra, and a Perkin-Elmer Model 237-B spectrophotometer for ir spectra.

The organic reagents and solvents (Aldrich Chemical Co., K & K Laboratories, Fisher Scientific, J. T. Baker Chemical Co., and Eastman Chemical Co.) were commercial compounds used without further purification. The KCN was ground and then dried under vacuum at 100° for 24 hr.

General Procedure. The starting solutions were prepared by weighing the reactive substrate directly into a 25-ml volumetric flask and diluting to the mark with a stock solution (known concentration)[15] of 1 in CH_3CN or C_6H_6. The prepared solutions were placed directly over solid, dry KCN (twofold excess of salt per functional group being displaced) and the reaction mixture was stirred vigorously at ambient or reflux temperature. Small aliquots of solution were removed at intervals and the extent of reaction was followed by glc and/or nmr analysis. Work-up involved separating the solid-liquid phases, removing the bulk of the solvent, diluting the remains with distilled water, extracting the product, and distilling the product after drying and removal of the extraction solvent.

1,4,7,10,13,16-Hexaoxacycloöctadecane (18-Crown-6,[3e] 1). The crown was synthesized and purified by a previously described procedure.[16]

Preparation of Nitrile Compounds. Preparation of 1,3-Dicyanopropane (Glutaronitrile, 2). A. Into a 50-ml round bottom flask equipped with a magnetic stirring bar and a condenser–drying tube system were placed 11.7 g (0.18 mol) of dry KCN (Fisher Scientific) and 25 ml of an acetonitrile solution containing 5.08 g (0.045 mol) of 1,3-dichloropropane (Aldrich Chemical Co.) and 1.01 g (0.0038 mol) of **1**. The two-phase system was heated to reflux with vigorous stirring and the extent of reaction was followed by glc techniques. After 1.5 hr, the reaction mixture was cooled, filtered, and evaporated to *ca.* one-third volume. Distilled water was then added, and the mixture was extracted with CH_2Cl_2.[17] The CH_2Cl_2 solution was dried over $MgSO_4$ and filtered, and the solvent was evaporated under reduced pressure. The residue was distilled under vacuum to give 4.10 g (96.8%) of **2**: bp 78–82° (0.15 mm); ir (neat, NaCl plates) 2950, 2875, 2240, 1450, 1420 cm^{-1}; ^1H nmr (neat, external TMS, $CHCl_3$) 2.65 (t, 4 H), 2.15 ppm ("spiked" q, 2 H); mass spectrum *m/e* 94, 93, 54, 41, 28; these spectra and glc analysis of the synthesized product corresponded to those of commercial **2** (K & K Laboratories).

Preparation of 1,2-Dicyanopropane (3). B. Into a 50-ml round-bottom flask equipped as in A were placed 0.32 g (0.005 mol) of dry KCN, 25 ml of an acetonitrile solution containing 3.03 g (0.045 mol) of methacrylonitrile (Eastman Chemical Co.) and 1.04 g (0.0039 mol) of **1**, and 4.42 g (0.052 mol) of acetone cyanohydrin (J. T. Baker Chemical Co.). The system was brought rapidly to reflux with vigorous stirring and the extent of reaction was monitored by glc and nmr techniques. After 0.6 hr, the system was cooled and the solution was worked up as in A.[17] Distillation of the isolated crude product[18] gave 3.89 g (91.9%) of the colorless, transparent liquid **3**: bp 68–71° (0.15 mm); ir (neat, NaCl plates) 2975, 2940, 2250, 1520, 1425, 1380 cm^{-1}; ^1H nmr (neat, external TMS, $CHCl_3$) 3.05 (m, 1 H), 2.65 (d, with spikes, 2 H), 1.35 ppm (d, 3 H); mass spectrum *m/e* 94, 93, 54, 41, 28.

Registry No.—Cyanide, 57-12-5; 18-crown-6, 17455-13-9; 1-octene, 111-66-0; *cis*-2-octene, 7642-04-8; *trans*-2-octene, 13389-42-9.

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(6) Monocyanated products could be isolated in the runs involving difunctional halides when the reactions were not allowed to proceed to completion.

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(8) The octenes produced in runs 16 and 17, Table I, were not isolated from the reaction mixtures. Low-temperature glc analysis revealed three alkenes to be present in both runs, assigned as 1-octene and *cis*- and *trans*-2-octene. The glc graphs were identical with that given by a known mixture of the three alkenes. Also, nmr splitting and position of the vinyl proton absorptions were overlapping with those of the known mixture.[9]

(9) The known mixture of octenes was supplied by Mr. H. P. Harris, and was isolated from the reaction of 2-bromooctane with "naked" fluoride.[7]

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(13) More recent advances than those listed[10] have shown that addition of catalytic amounts of iodide to the ethanol–water system has a beneficial effect on nucleophilic displacements of alkyl halides. H. O. House, *Org. React.*, **9**, 139 (1957), and references cited therein.

(14) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 9, pp 623–628, and references cited therein.

(15) It has been found that the upper limit of concentration of **1** in CH_3CN is approximately 0.2 *M* at room temperature, while concentrations as high as 1.5 *M* have easily been achieved in C_6H_6.[1]

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(17) Extraction of the nitrile compounds can be accomplished by hand (three to five extractions) or by a CH_2Cl_2 continuous extractor (20–24 hr). As nitriles are soluble in H_2O (especially dinitriles) to various extents, the continuous-extraction method is recommended in cases where small quantities are involved and complete extraction from the water layer is desired. For larger runs, the hand-extraction technique is preferred. Both methods were used with comparable results in preparing this report.

(18) On evaporation of the extraction solvent, the crystalline adduct (complex) of **7** and **1** precipitates spontaneously. However, on heating the distillation flask the complex readily melts, and the liquid **7** is then easily distilled. The characteristics of this and a number of other crystalline complexes of nitrile compounds and **1** have been reported: F. L. Cook, H. P. Harris, and C. L. Liotta, *J. Org. Chem.*, submitted for publication.

VITA

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